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(54) HPPD variants and methods of use

(57) The present invention relates to an isolated nucleic acid comprising a nucleotide sequence encoding a mutated HPPD protein, wherein said mutated HPPD protein has HPPD activity, wherein in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises at least one amino acid selected from certain amino acids at specific positions important for conferring an increased HPPD inhibitor tolerance. The present invention also relates to proteins encoded by the nucleic acid of the invention, to chimeric genes, plant cells comprising the nucleic acid of the invention operably linked to a plant-expressible promoter and optionally a transcription termination and polyadenylation region, plants essentially consisting of the plant cells of the invention and methods of obtaining transgenic plants.

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Description

[0001] The present invention relates to an isolated nucleic acid comprising a nucleotide sequence encoding a mutated HPPD protein, wherein said mutated HPPD protein has HPPD activity, wherein in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises at least one amino acid selected from certain amino acids at specific positions important for conferring an increased HPPD inhibitor tolerance. The present invention also relates to proteins encoded by the nucleic acid of the invention, to chimeric genes, plant cells comprising the nucleic acid of the invention operably linked to a plant-expressible promoter and optionally a transcription termination and polyadenylation region, plants essentially consisting of the plant cells of the invention and methods of obtaining transgenic plants.

[0002] In this specification, a number of documents including patent applications and manufacturer's manuals are cited. The disclosure of these documents, while not considered relevant for the patentability of this invention, is herewith incorporated by reference in its entirety. More specifically, all referenced documents are incorporated by reference to the same extent as if each individual document was specifically and individually indicated to be incorporated by reference.

[0003] HPPD (hydroxyphenylpyruvate dioxygenase) proteins are enzymes which catalyse the reaction in which para-hydroxyphenylpyruvate (abbreviated herein as HPP), a tyrosine degradation product, is transformed into homogentisate (abbreviated herein as HG), the precursor in plants of tocopherol and plastoquinone (Crouch N.P. et al. (1997) Tetrahedron, 53, 20, 6993-7010, Fritze et al., (2004), Plant Physiology 134:1388-1400). Tocopherol acts as a membrane-associated antioxidant. Plastoquinone, firstly acts as an electron carrier between PSII and the cytochrome b6/f complex and secondly, is a redox cofactor for phytoene desaturase, which is involved in the biosynthesis of carotenoids.

[0004] Up to now, more than 700 nucleic acid sequences from various organisms present in NCBI database were annotated as coding for a putative protein having an HPPD domain. But for most of these sequences, it has not been proven that the protein would have an HPPD enzymatic activity either in an *in vitro* assay or an in *in planta* approach, nor that such HPPD protein can confer herbicide tolerance to HPPD inhibitor herbicides when expressed in a plant. Several HPPD proteins and their primary sequences have been described in the state of the art, in particular the HPPDs of bacteria such as *Pseudomonas* (Rüetschi et al Eur. J. Biochem., 205, 459-466, 1992, WO 96/38567), of plants such as *Arabidopsis* (WO 96/38567, Genebank AF047834), carrot (WO 96/38567, Genebank 87257), *Avena sativa* (WO 02/046387), wheat (WO 02/046387), *Brachiaria platyphylla* (WO 02/046387), *Cenchrus echinatus* (WO 02/046387), *Lolium rigidum* (WO 02/046387), *Festuca arundinacea* (WO 02/046387), *Setaria faberi* (WO 02/046387), *Eleusine indica* (WO 02/046387), *Sorghum* (WO 02/046387), *Coccicoides* (Genebank COITRP),of *Coptis japonica* (WO 06/132270), *Chlamydomonas reinhardtii* (ES 2275365), or of mammals such as mouse or pig.

[0005] Most plants synthesize tyrosine via arrogenate (Abou-Zeid et al. (1995), Applied Env Microb 41: 1298-1302; Bonner et al., (1995), Plant Cells Physiol. 36, 1013-1022; Byng et al., (1981), Phytochemistry 6: 1289-1292; Connely and Conn (1986), Z. Naturforsch 41 c: 69-78; Gaines et al., (1982), Plants 156: 233-240). In these plants, the HPP is derived only from the degradation of tyrosine. On the other hand, in organisms such as the yeast *Sacharomyces cerevisiae* or the bacterium *Escherichia coli,* HPP is a tyrosine precursor, and it is synthesized by the action of an enzyme, prephenate dehydrogenase (hereinafter referred to as PDH), which converts prephenate to HPP (Lingens et al., (1967) European J. Biochem 1: 363-374; Sampathkumar and Morrisson (1982), Bioch Biophys Acta 701: 204-211). In these organisms, the production of HPP is therefore directly connected to the aromatic amino acid biosynthetic pathway (shikimate pathway), and not to the tyrosine degradation pathway.

[0006] Inhibition of HPPD leads to uncoupling of photosynthesis, deficiency in accessory light-harvesting pigments and, most importantly, to destruction of chlorophyll by UV-radiation and reactive oxygen species (bleaching) due to the lack of photo protection normally provided by carotenoids (Norris et al. (1995), Plant Cell 7: 2139-2149). Bleaching of photosynthetically active tissues leads to growth inhibition and plant death.

[0007] At present, most commercially available HPPD inhibitor herbicides belong to one of these four chemical families:

1) the triketones, e.g. sulcotrione [i.e. 2-[2-chloro-4-(methylsulfonyl)benzoyl]-1,3-cyclohexanedione], mesotrione [i.e.2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione]; tembotrione [i.e.2-[2-chloro-4-(methylsulfonyl)-3-[(2,2,2,-trifluoroethoxy)methyl] benzoyl]-1,3-cyclo-hexanedione]; tefuryltrione [i.e. 2-[2-chloro-4-(methylsulfonyl)-3-[[(tetrahydro-2-furanyl)methoxy]methyl]benzoyl]-1,3 cyclohexanedione]]; bicyclopyrone [i.e. 4-hydroxy-3-[[2-[(2-methoxyethoxy)methyl]-6-(trifluoromethyl)-3-pyridinyl]carbonyl]bicyclo[3.2.1]oct-3-en-2-one] ; Benzobicyclon [i.e. 3-(2-chloro-4-mesylbenzoyl)-2-phenylthiobicyclo[3.2.1]oct-2-en-4-one]

2) The diketonitriles, e.g. 2-cyano-3-cyclopropyl-1-(2-methylsulphonyl-4-trifluoromethylphenyl)-propane-1,3-dione and 2-cyano-1-[4-(methylsulphonyl)-2-trifluoromethylphenyl]-3-(1-methylcyclopropyl)propane-1,3-dione;

3) the isoxazoles, e.g. isoxaflutole [i.e.(5-cyclopropyl-4-isoxazolyl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl] methanone]. In plants, the isoxaflutole is rapidly metabolized in DKN, a diketonitrile compound which exhibits the

HPPD inhibitor property; and

4) the pyrazolinates, e.g. topramezone [i.e.[3-(4,5-dihydro-3-isoxazolyl)-2-methyl-4-(methylsulfonyl) phenyl](5-hydroxy-1-methyl-1 H-pyrazol-4-yl)methanone], and pyrasulfotole [(5-hydroxy-1,3-dimethylpyrazol-4-yl(2-mesyl-4-trifluaromethylphenyl)methanone]; pyrazofen [2-[4-(2,4-dichlorobenzoyl)-1,3-dimethylpyrazol-5-yloxy]acetophenone].

[0008] These HPPD-inhibiting herbicides can be used against grass and/or broad leaf weeds in crop plants that display metabolic tolerance, such as maize (Zea mays) in which they are rapidly degraded (Schulz et al., (1993). FEBS letters, 318, 162-166; Mitchell et al., (2001) Pest Management Science, Vol 57, 120-128; Garcia et al., (2000) Biochem., 39, 7501-7507; Pallett et al., (2001) Pest Management Science, Vol 57, 133-142). In order to extend the scope of these HPPD-inhibiting herbicides, several efforts have been developed in order to confer to plants, particularly plants without or with an underperforming metabolic tolerance, a tolerance level acceptable under agronomic field conditions.

[0009] Besides the attempt of by-passing HPPD-mediated production of homogentisate (US 6,812,010), overexpressing the sensitive enzyme so as to produce quantities of the target enzyme in the plant which are sufficient in relation to the herbicide has been performed (WO96/38567). Overexpression of HPPD resulted in better pre-emergence tolerance to the diketonitrile derivative (DKN) of isoxaflutole (IFT), but tolerance was not sufficient for tolerance to post-emergence treatment (Matringe et al., (2005), Pest Management Science 61: 269-276).

[0010] In WO 04/024928, the inventors have sought to increase the prenylquinone biosynthesis (e.g., synthesis of plastoquinones, tocopherols) in the cells of plants by increasing the flux of the HPP precursor into the cells of these plants. This has been done by connecting the synthesis of said precursor to the "shikimate" pathway by overexpression of a PDH enzyme. They have also noted that the transformation of plants with a gene encoding a PDH enzyme makes it possible to increase the tolerance of said plants to HPPD inhibitors.

[0011] Another strategy was to mutate the HPPD in order to obtain a target enzyme which, while retaining its properties of catalysing the transformation of HPP into homogentisate, is less sensitive to HPPD inhibitors than is the native HPPD before mutation.

[0012] This strategy has been successfully applied for the production of plants tolerant to 2-cyano-3-cyclopropyl-1-(2-methylsulphonyl-4-trifluoromethylphenyl)-propane-1,3-dione and to 2-cyano-1-[4-(methylsulphonyl)-2-trifluoromethylphenyl]-3-(1-methylcyclopropyl)propane-1,3-dione (EP496630), two HPPD-inhibiting herbicides belonging to the diketonitriles family (WO 99/24585). Pro215Leu, Gly336Glu, Gly336Ile, and more particularly Gly336Trp (positions of the mutated amino acid are indicated with reference to the *Pseudomonas* HPPD) were identified as mutations which are responsible for an increased tolerance to pre-emergence treatment with these diketonitrile herbicides without causing an alteration of the activity of the enzyme.

[0013] More recently, introduction of a *Pseudomonas* HPPD gene into the plastid genome of tobacco and soybean has shown to be more effective than nuclear transformation, conferring even tolerance to post-emergence application of isoxaflutole (Dufourmantel et al., 2007, Plant Biotechnol J.5(1):118-33).

[0014] In the patent application WO 2009/144079, a nucleic acid sequence encoding a mutated hydroxyphenylpyruvate dioxygenase (HPPD) at position 336 of the *Pseudomonas fluorescens* HPPD protein and its use for obtaining plants which are tolerant to HPPD inhibitor herbicides is disclosed.

[0015] In WO 2002/046387, several domains of HPPD proteins originated from plants have been identified that may be relevant to confer tolerance to various HPPD inhibitor herbicides but no *in planta* nor biochemical data have been shown to confirm the impact of the as described domain functions.

[0016] In WO 2008/150473, the combination of two distinct tolerance mechanisms - a modified *Avena sativa* gene coding for a mutant HPPD enzyme and a CYP450 Maize monooxygenase (nsf1 gene) - was exemplified in order to obtain an improved tolerance to HPPD inhibitor herbicides, but no data have been disclosed demonstrating the synergistic effects based on the combination of both proteins.

[0017] US 2010/0197503 suggests a number of mutations at different positions within or close to the active site of the HPPD taken from Avena sativa and examined some of them for their inhibition by certain HPPD inhibitors such as sulcotrione in vitro and in planta.

[0018] Despite these successes obtained for the development of plants showing tolerance to several HPPD inhibitors herbicides described above, it is still necessary to develop and/or improve the tolerance of plants to newer or to several different HPPD inhibitors, particularly HPPD inhibitors belonging to the classes of the triketones (e.g.sulcotrione, mesotrione, tembotrione, benzobicyclon and bicyclopyrone) and the pyrazolinates (e.g., topramezone and pyrasulfotole).

[0019] Accordingly, the present invention relates to an isolated nucleic acid comprising a nucleotide sequence encoding a mutated HPPD protein, wherein said mutated HPPD protein has HPPD activity, wherein in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises at least one amino acid selected from:

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile, Leu or Met at a position in an HPPD protein, said position corresponding to position 250 of the amino acid sequence of SEQ ID No. 2;
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg,Ser Gly, His or Tyr" at a position in an HPPD protein, said position corresponding to position 251 of the amino acid sequence of SEQ ID No. 2;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No.;
d) Ala, Phe, His, Gln, Val, Trp, Ile, Leu or Met at a position in an HPPD protein, said position corresponding to position 253 of the amino acid sequence of SEQ ID No. 2;
e) Leu, Val, or Met at a position in an HPPD protein, said position corresponding to position 265 of the amino acid sequence of SEQ ID No. 2;
f) Leu, Gln, Arg, Val, Tyr, Ala, Ile, Lys or Met at a position in an HPPD protein, said position corresponding to position 268 of the amino acid sequence of SEQ ID No. 2;
g) Ala, Thr or Val at a position in an HPPD protein, said position corresponding to position 269 of the amino acid sequence of SEQ ID No. 2;
h) Ala, Ile, Asn, Pro, Thr or Val at a position in an HPPD protein, said position corresponding to position 280 of the amino acid sequence of SEQ ID No. 2;
i) Leu, Gln, Val, Ala, Phe, Gly, Met, Arg or Ser at a position in an HPPD protein, said position corresponding to position 293 of the amino acid sequence of SEQ ID No. 2;
j) Ile, Met, Ala, Pro, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 294 of the amino acid sequence of SEQ ID No. 2;
k) Gln, His or Asn at a position in an HPPD protein, said position corresponding to position 307 of the amino acid sequence of SEQ ID No. 2;
l) Ile, Met, Asn or Leu at a position in an HPPD protein, said position corresponding to position 335 of the amino acid sequence of SEQ ID No. 2;
m) Leu or Met at a position in an HPPD protein, said position corresponding to position 368 of the amino acid sequence of SEQ ID No. 2;
n) Phe or Tyr at a position in an HPPD protein, said position corresponding to position 381 of the amino acid sequence of SEQ ID No. 2;
o) Phe or Ser at a position in an HPPD protein, said position corresponding to position 392 of the amino acid sequence of SEQ ID No. 2;
p) Phe or Tyr at a position in an HPPD protein, said position corresponding to position 419 of the amino acid sequence of SEQ ID No. 2;
q) Asp, Lys, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 421 of the amino acid sequence of SEQ ID No. 2;
r) Ala, Gly, Met, Pro or Thr at a position in an HPPD protein, said position corresponding to position 422 of the amino acid sequence of SEQ ID No. 2;
s) Ala, Phe, Ile or Val at a position in an HPPD protein, said position corresponding to position 424 of the amino acid sequence of SEQ ID No. 2;
t) Ile, Pro, Arg, Ser Ala, Gly, Lys, Asn or Gln at a position in an HPPD protein, said position corresponding to position 425 of the amino acid sequence of SEQ ID No. 2;
u) Glu, Phe, Thr, Val Ala, Gln or Ser at a position in an HPPD protein, said position corresponding to position 426 of the amino acid sequence of SEQ ID No. 2;
v) Ile, Met, Gln, Val Phe or Leu at a position in an HPPD protein, said position corresponding to position 431 of the amino acid sequence of SEQ ID No. 2; and
w) at least one amino acid deletion or replacement at any one of positions 228, 248, 270, 271, 379 and/or 427.

[0020] Unless indicated otherwise, the specific definitions or specific features of certain embodiments can be introduced into any other embodiment of the present invention.

[0021] According to the present invention, a "nucleic acid" is understood as being a nucleotide sequence which can be of the DNA or RNA type, preferably of the DNA type, and in particular double-stranded, whether it be of natural or synthetic origin, in particular a DNA sequence in which the codons which encode the HPPD according to the invention have been optimized in accordance with the host organism in which it is to be expressed (e.g., by replacing codons with those codons more preferred or most preferred in codon usage tables of such host organism or the group to which such host organism belongs, compared to the original or source organism).

[0022] An "isolated nucleic acid/DNA/protein", as used in the present application, refers to a nucleic acid/DNA/protein which is not naturally-occurring (such as an artificial or synthetic DNA with a different nucleotide sequence than the naturally-occurring DNA, or a modified protein) or which is no longer in the natural environment wherein it was originally present, e.g., a DNA coding sequence associated with a heterologous regulatory element (such as a bacterial coding sequence operably-linked to a plant-expressible promoter) in a chimeric gene, a DNA transferred into another host cell, such as a transgenic plant cell.

[0023] The terminology relating to nucleic acid or protein "comprising" a certain nucleotide sequence or amino acid sequence, as used throughout the text, refers to a nucleic acid or protein including or containing at least the described sequence, so that other nucleotide or amino acid sequences can be included at the 5' (or N-terminal) and/or 3' (or C-terminal) end, e.g. (the nucleotide sequence of) a selectable marker protein, (the nucleotide sequence of) a transit peptide, and/or a 5' leader sequence or a 3' trailer sequence. Similarly, use of the term "comprise", "comprising" or "comprises" throughout the text and the claims of this application should be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps. The term "comprising" also includes the term "consisting of".

[0024] In accordance with the present invention, the term "mutated HPPD protein" which is interchangeably used with the term "mutant HPPD protein" denotes an HPPD protein having an amino acid sequence which does not occur in nature. As opposed to the term "isolated" referred to above, the term "mutated" cannot refer to the environment of the (amino acid or protein) sequence in question, such as it being isolated from its natural environment or being coupled to a heterologous (amino acid or protein) sequence, but only refers to the amino acid sequence defining said mutated HPPD protein which cannot be found anywhere in nature but arose from a unmutated or wild-type starting amino acid sequence. In other words, in arriving at the nucleic acid of the present invention encoding a mutated HPPD protein, a starting amino acid sequence of a naturally existing protein has to be taken and to be modified by man by replacing at least one amino acid as defined in the present application.

[0025] The sequence which encodes an original unmutated HPPD which will be mutated according to the invention can be of any origin. In particular, it can be of bacterial, plant or animal origin. Advantageous examples which may be cited are bacteria of the Pseudomonas sp. type, for example Pseudomonas fluorescens, or otherwise cyanobacteria of the Synechocystis genus. The sequence can also be of plant origin, in particular derived from dicotyledonous plants, umbelliferous plants, or otherwise monocotyledonous plants. Advantageous examples which may be cited are plants such as tobacco, Arabidopsis, Daucus carotta, Zea mays (corn), wheat, barley, Avena sativa, wheat, Brachiaria platyphylla, Cenchrus echinatus, Lolium rigidum, Festuca arundinacea, Setaria faberi, Eleusine indica, and Sorghum. The coding sequences, and the way of isolating and cloning them, are described in the previously cited references. In a particular embodiment of the invention, the HPPD is from a bacterial origin, particularly from Pseudomonas sp., more particularly from Pseudomonas fluorescens, Rhodococcus sp., Blepharisma japonicum, Synechococcus sp., Picrophilus torridus, Kordia algicida or from a plant origin, particularly from Arabidopsis thaliana or Avena sativa. The HPPD to make the mutation (s) in for the purpose of the invention, can be any naturally-occurring HPPD, or any active fragment thereof or any variant thereof wherein some amino acids (1 to 10 amino acids) have been replaced, added or deleted for cloning purposes, to make a transit peptide fusion, and the like, which retains HPPD activity, i.e. the property of catalysing the conversion of para-hydroxyphenylpyruvate to homogentisate.

[0026] The mutated HPPD protein according to the present invention has HPPD activity, i. e., as described above, catalyses the reaction in which para-hydroxyphenylpyruvate is transformed into homogentisate. Preferentially, the catalytic activity of the isolated mutated HPPD of the present invention, when tested in vitro, does not differ from that of the unmutated reference HPPD protein by more than 70%, preferably more than 50%, more preferably more than 30%, even more preferably more than 20% when assayed under identical conditions and in the absence of the HPPD inhibitor herbicides described above. The catalytic activity of an HPPD enzyme may be defined by various methods well-known in the art. WO 2009/144079 describes various suitable screening methods.

[0027] Initial screens may be performed with the nucleic acid encoding the mutated HPPD protein of the invention being expressed in bacteria.

[0028] Colorimetric Screening Test for Active HPPD Enzymes:

> A YT-broth-type culture medium with 1% agarose, 5mM L-Tyrosine and 42mM Succinate, which contains the selection agent for the vector pSE420 (Invitrogen, Karlsruhe, Germany) is poured into deep well plates. E.coli culture in the exponentional growth phase which contains the vector pSE420-HPPDx (HPPDx means any gene coding for a putative HPPD enzyme/protein) is applied to each well.
>
> After 16 hours at 37°C, the wells which do not contain the culture medium, those which have been seeded with an E. coil culture containing the empty vector pSE420 are transparent, or those which have been seeded with an E. coli culture containing a vector pSE420-HPPDx containing a gene coding for an inactive HPPD are transparent, while the weels seeded with an E. coli culture containing the vector pSE420-HPPDx coding for an active HPPD are brown. It has been previously demonstrated that this test refelects the HPPD activity, whatever the orgin of this activity is, and allows the identification of HPPD activities (US 6,768,044), i.e. at a qualitative level.

[0029] Further and more elaborate screens may be carried out in plant cells or plants expressing the mutated HPPD protein of the invention.

[0030] The same screenings may also be used when examining of whether a mutated HPPD protein is capable of modulating, such as decreasing or increasing, the tolerance of a plant to at least one HPPD herbicide inhibitor which will be referred to further below, with the difference that at least one of such an HPPD inhibitor is added. Examples of HPPD inhibitors to be used in those screenings include tembotrione, mesotrione, pyrasulfotole, bicyclopyrone, topramezone and sulcotrione. A screening method which is simple to implement is to determine the dose of HPPD inhibitor which fully inhibits the original unmutated HPPD, and which is lethal for the cells which express this unmutated HPPD, and to subject the mutated cells to this predetermined dose, and thereafter to isolate the mutated cells which have withstood this lethal dose, and then to isolate and to clone the gene which encodes the mutated HPPD.

[0031] Alternatively, at the quantitative level data like pI_{50} (pI_{50}-value means the log value of the concentration of inhibitor necessary to inhibit 50% of the enzyme activity in molar concentration) can be obtained by employing the isolated and purified HPPD polypeptide, i.e. the mutated vs. the unmutated HPPD polypeptide and in presence or absence of the any respective HPPD inhibitor herbicide.

[0032] The terms "tolerance", "tolerant" or "less sensitive" denotes the lack of susceptibility of a plant expressing the mutated HPPD protein of the present invention to substances, particularly herbicides, which inhibit HPPD proteins, optionally in comparison with the plant's own HPPD protein or with any known HPPD protein. More specifically, said terms mean the relative levels of inherent tolerance of the HPPD screened according to a visible indicator phenotype of the strain or plant transformed with a nucleic acid comprising the gene coding for the respective HPPD protein in the presence of different concentrations of the various HPPD inhibitors. Dose responses and relative shifts in dose responses associated with these indicator phenotypes (formation of brown colour, growth inhibition, bleaching, herbicidal effect etc) are conveniently expressed in terms, for example, of GR50 (concentration for 50% reduction of growth) or MIC (minimum inhibitory concentration) values where increases in values correspond to increases in inherent tolerance of the expressed HPPD, in the normal manner based upon plant damage, meristematic bleaching symptoms etc. at a range of different concentrations of herbicides. These data can be expressed in terms of, for example, GR50 values derived from dose/response curves having "dose" plotted on the x-axis and "percentage kill", "herbicidal effect", "numbers of emerging green plants" etc. plotted on the y-axis where increased GR50 values correspond to increased levels of inherent tolerance of the expressed HPPD. Herbicides can suitably be applied pre-emergence or post emergence.

[0033] Likewise, tolerance level of the nucleic acid or gene encoding an HPPD protein according to the invention, or the mutated HPPD protein of the invention is screened via transgenesis, regeneration, breeding and spray testing of a test plant such as tobacco, or a crop plant such as soybean or cotton. In line with the results obtained by such screening, such plants are at least 2-4 times more tolerant to HPPD inhibitors like tembotrione, mesotrione, diketonitrile, and/or bicyclopyrone, pyrasulfotole, than plants that do not contain any exogenous gene encoding an HPPD protein, or than plants that contain a gene comprising an *Arabidopsis thaliana* HPPD-encoding DNA, under control of the same promoter as the nucleic acid encoding the mutated HPPD protein of the invention. Accordingly, the term "capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD" denotes a tolerance increased in a plant by at least the factor of 2, alternatively at least the factor of 3 or 4 or even 5 or 6 as compared to a plant only expressing it's endogenous HPPD or a plant expressing an Arabidopsis thaliana HPPD. In this regard, the term "herbicide acting on HPPD" is not limited to substances which are known and/or used as herbicides but to any substances which inhibits the catalytic activity of HPPD proteins.

[0034] In an alternative embodiment of the nucleic acid encoding a mutated HPPD polypeptide comprising at least one of the mutations as defined above, the HPPD protein comprises

a) a His at a position in an HPPD protein, said position corresponding to position 226 of the amino acid sequence of SEQ ID No. 2;
b) a Ser at a position in an HPPD protein, said position corresponding to position 267 of the amino acid sequence of SEQ ID No. 2;
c) an Asn at a position in an HPPD protein, said position corresponding to position 282 of the amino acid sequence of SEQ ID No. 2;
d) a His at a position in an HPPD protein, said position corresponding to position 308 of the amino acid sequence of SEQ ID No. 2;
e) a Tyr at a position in an HPPD protein, said position corresponding to position 342 of the amino acid sequence of SEQ ID No. 2;
f) a Glu at a position in an HPPD protein, said position corresponding to position 394 of the amino acid sequence of SEQ ID No. 2;
g) a Gly at a position in an HPPD protein, said position corresponding to position 420 of the amino acid sequence of SEQ ID No. 2; and
h) an Asn at a position in an HPPD protein, said position corresponding to position 423 of the amino acid sequence of SEQ ID No. 2

[0035] In the mutated HPPD protein encoded by the nucleic acid of the invention at least one amino acid has been deleted or replaced as defined above.

[0036] The replacement or deletion can be effected in the nucleic acid sequence which encodes the original unmutated, i. e. naturally occurring HPPD as defined above by any means which is appropriate for replacing, in the said sequence, the codon which encodes the amino acid to be replaced with the codon which corresponds to the amino acid which is to replace it, or by deleting a codon, with the said codons being widely described in the literature and well known to the skilled person. Several molecular biological methods can be used to achieve this replacement or deletion. A preferred method for preparing a mutated nucleic acid sequence according to the invention and the corresponding protein comprises carrying out site-directed mutagenesis on codons encoding one or more amino acids which are selected in advance. The methods for obtaining these site-directed mutations are well known to the skilled person and widely described in the literature (in particular: Directed Mutagenesis: A Practical Approach, 1991, Edited by M.J. McPHERSON, IRL PRESS), or are methods for which it is possible to employ commercial kits (for example the U. S. E. mutagenesis kit from PHARMACIA). After the site-directed mutagenesis, it is useful to select the cells which contain a mutated HPPD which is less sensitive to an HPPD inhibitor by using an appropriate screening aid. Appropriate screening methods to achieve this have been described above.

[0037] In accordance with the present invention, the term "said position corresponding to position X", X being any number to be found in the respective context in the present application, does not only include the respective position in the SEQ ID No. referred to afterwards but also includes any sequence encoding an HPPD protein, where, after alignment with the reference SEQ ID No., the respective position might have a different number but corresponds to that indicated for the reference SEQ ID No. Whereas HPPD sequences may be very diverse and may only show a low sequence identity of about 30%, HPPD proteins are characterized by a common three dimensional consensus structure which is achieved despite a low sequence identity. Due to specific positions being conserved within HPPD proteins, alignment of HPPD proteins can be effected by by applying various alignment tools in a senseful manner. Methods of aligning nucleic acid or amino acid sequences and, accordingly, determining the sequence identity of two or more sequences, are well-known in the art. They include performing mathematical algorithms such as the algorithm of Myers and Miller (1988) CABIOS 4:11-17 or the local alignment algorithm of Smith and Waterman (1981) Adv. Appl. Math. 2:482-489; the global alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48:443-453; the algorithm of Karlin and Altschul (1990) Proc. Natl. Acad. Sci USA 872264 and that of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990)).

[0038] Such algorithms can be implemented in computer programs including but not limited to CLUSTALX, ALIGN, GAP, BESTFIT, BLAST, FASTDB and FASTA.

[0039] For example, when using BESTFIT (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, WI 53711)or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence, the parameters are set, of course, such that the percentage of identity is calculated over the full length of the reference nucleotide sequence and that gaps in homology of up to 5% of the total number of nucleotides in the reference sequence are allowed.

[0040] The identity between a first sequence and a second sequence, also referred to as a global sequence alignment, is determined using the FASTDB computer program based on the algorithm of Brutlag and colleagues (Comp. App. Biosci. 6:237-245 (1990)). In a sequence alignment the query and subject sequences are both DNA sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

[0041] The present invention is based on the results of a combination of a comparison of the amino acid sequences of HPPD proteins from various organisms and the analysis of the substrate binding and inhibitor binding site of selected HPPD proteins using X-ray crystallography. Using this combined approach, it was possible to determine key positions in HPPD proteins, where an amino acid can be replaced with one of a defined set of other amino acids in order to modulate HPPD catalytic activity and the affinity to at least one HPPD herbicide inhibitor to a plant expressing the mutated HPPD protein.

[0042] Superposition of the 3D structure of HPPD from *Arabidopsis thaliana* (1TFZ) (Yang et al., 2004, Biochemistry 43, 10414-10423) with the 3D structures of HPPD from other species such as *Pseudomonas fluorescens* (1CJX) (Serre et al., 1999, Structure Fold Des. 7, 977-988), *Streptomyces avermitilis* (1T47) (Brownlee et al., 2004, Biochemistry 43, 6370-6377), *Homo sapiens* (3ISQ) (PDB ID: 3isq Pilka et al., Structural Genomics Consortium (SGC). Crystal structure of human 4-Hydroxyphenylpyruvate dioxygenase), *Rattus norvegicus* (1SQI) (Yang et al., 2004, Biochemistry 43, 10414-10423) shows that they have the same folding and corresponding amino acids are at equivalent position in the 3D structure of the protein. Since the species with known 3D structures are very diverse in their amino acid sequence, it can be assumed that all HPPD sequences have the same basic folding even though the overall sequence identity is low. The sequence and the 3D structure of *Arabidopsis thaliana* has been used as reference structure in the present invention. Figure 1 shows the superposition of the structure of A.thaliana HPPD with the structure of (a) *Pseudomonas* *fluorescens,* (b) *Streptomyces avermitilis,* (c) *Homo sapiens* and (d) *Rattus norvegicus.* In order to define the binding site of the substrate and/or inhibitors, amino acids were selected which play a role in catalysis or inhibitor binding. This includes amino acids in the active site and amino acids from the C-terminal helix. The 3D arrangement is demonstrated in Figure 2 which displays the amino acids defined as binding site in case of (a) *Arabidopsis thaliana,* (b) *Pseudomonas fluorescens,* (c) *Streptomyces avermitilis,* (d) *Homo sapiens* and (e) *Rattus norvegicus.* The amino acid numbering of the *Pseudomonas Fluorescens structure* (1 cjx) was changed into the numbering according to SEQ ID No. 10. The 36 amino acids defining the binding site including their position are listed in Table 1 for (a) *Arabidopsis thaliana,* (b) *Pseudomonas fluorescens,* (c) *Streptomyces avermitilis,* (d) *Homo sapiens* and (e) *Rattus norvegicus.*

Table 1: Amino acids forming the binding site in A.thaliana, P.fluorescens, S.avermitilis, H.sapiens, R. norvegicus

Arabidopsis thaliana		*Pseudomonas fluorescens*		*Streptomyces avermitilis*		*Homo sapiens*		*Rattus norvegicus*	
Position	Amino Acid	Position	Amino Acid	Position	Amino Acid	Position	Amino Acid	Position	Amino Acid
226	H	162	H	187	H	183	H	183	H
228	V	164	T	189	V	185	V	185	V
248	H	186	R	211	T	207	H	207	H
250	F	188	A	213	M	209	F	209	F
251	A	189	R	214	K	210	W	210	W
252	E	190	Y	215	E	211	S	211	S
253	F	191	F	216	F	212	V	212	V
265	L	200	L	228	L	224	L	224	L
267	S	202	S	230	S	226	S	226	S
268	A	203	K	231	K	227	I	227	I
269	V	204	A	232	V	228	V	228	V
270	L	205	M	233	V	229	V	229	V
271	A	206	S	234	A	230	A	230	A
280	P	215	P	243	P	239	P	239	P
282	N	217	N	245	N	241	N	241	N
293	Q	226	Q	255	Q	251	Q	251	Q
294	1	227	I	256	I	252	I	252	I
307	Q	240	Q	269	Q	265	Q	265	Q
308	H	241	H	270	H	266	H	266	H
335	M	264	M	293	L	289	L	289	L
342	Y	271	Y	299	Y	295	Y	295	Y
368	L	295	L	323	L	323	L	323	L
379	Q	310	Q	334	Q	334	Q	334	Q
381	F	312	F	336	F	336	F	336	F
392	F	321	F	347	F	347	F	347	F
394	E	323	E	349	E	349	E	349	E
419	F	333	F	359	F	359	F	359	F
420	G	334	G	360	G	360	G	360	G
421	K	335	E	361	K	361	A	361	A
422	G	336	G	362	G	362	G	362	G
423	N	337	N	363	N	363	N	363	N
424	F	338	F	364	F	364	F	364	F
425	S	339	K	365	K	365	N	365	N
426	E	340	A	366	A	366	S	366	S
427	L	341	L	367	L	367	L	367	L
431	I	345	I	371	I	371	F	371	F

[0043] An exemplary alignment of HPPD proteins is given in Table 2a for the HPPD proteins with known 3D structures.

Table 2a gives the numbering of the amino acids of the Arabidopsis sequence and also the amino acids which are common within these HPPD sequences, with these amino acids being designated by an asterisk. On the basis of such an alignment and from the definition of the Arabidopsis amino acid by its position and its nature, it is easy to identify the position of the corresponding amino acid in another HPPD sequence. Figure 2 shows that this can be done with the alignment of sequences of different plant, mammalian and bacterial origin, demonstrating that this method of alignment, which is well known to a skilled person, can be generalized to any other sequence. An alignment of different HPPD sequences is also described in Patent Application WO 97/49816.

Table 2a: Alignment of HPPD sequences with known crystal structures i.e. A.thaliana, P.fluorescens, S.avermitilis, H.sapiens, R. norvegicus

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
1	M		-		-		-			
2	G		-		-		-			
3	H		-		-		-			
4	Q		-		-		-			
5	N		-		-		-			
6	A		-		-		-			
7	A		-		-		-			
8	V		-		-		-			
9	S		-		-		-			
10	E		-		-		-			
11	N		-		-		-			
12	Q		-		-		-			
13	N		-		-		-			
14	H		-	1	M		-			
15	D		-	2	T		-			
16	D		-	3	Q		-			
17	G		-	4	T		-			
18	A		-	5	T		-			
19	A		-	6	H	8	G	8	G	
20	S		-	7	H	9	A	9	P	
21	S		-	8	T	10	K	10	K	
22	P		-	9	P	11	P	11	P	
23	G		-		-		-			
24	F		-		-		-			
25	K		-		-		-			
26	L		-		-		-			
27	V		-		-		-			
28	G		-		-		-			
29	F		-		-		-			

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
30	S		-		-		-			
31	K		-		-		-			
32	F		-		-		-			
33	V		-		-		-			
34	R		-	10	D	12	E	12	E	
35	K	2	A	11	T	13	R	13	R	
36	N	3	D	12	A	14	G	14	G	
37	P	4	L	13	R	15	R	15	R	
38	K	5	Y	14	Q	16	F	16	F	
39	S	6	E	15	A	17	L	17	L	
40	D	7	N	16	D	18	H	18	H	
41	K	8	P	17	P		-			
42	F	9	M	18	F		-			
43	K	10	G	19	P		-			
44	V	11	L	20	V		-			
45	K	12	M	21	K		-			
46	R	13	G	22	G		-			
47	F	14	F	23	M	19	F	19	F	
48	H	15	E	24	D	20	H	20	H	
49	H	16	F	25	A	21	S	21	S	
50	I	17	I	26	V	22	V	22	V	
51	E	18	E	27	V	23	T	23	T	
52	F	19	F	28	F	24	F	24	F	X
53	W	20	A	29	A	25	W	25	W	
54	C	21	S	30	V	26	V	26	V	
55	G	22	P	31	G	27	G	27	G	
56	D	23	T	32	N	28	N	28	N	
57	A	24	P	33	A	29	A	29	A	
58	T	25	G	34	K	30	K	30	K	
59	N	26	T	35	Q	31	Q	31	Q	
60	V	27	L	36	A	32	A	32	A	
61	A	28	E	37	A	33	A	33	A	
62	R	29	P	38	H	34	S	34	S	
63	R	30	I	39	Y	35	F	35	F	
64	F	31	F	40	Y	36	Y	36	Y	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
65	S	32	E	41	S	37	C	37	C	
66	W	33	I	42	T	38	S	38	N	
67	G	34	M	43	A	39	K	39	K	
68	L	35	G	44	F	40	M	40	M	
69	G	36	F	45	G	41	G	41	G	
70	M	37	T	46	M	42	F	42	F	
71	R	38	K	47	Q	43	E	43	E	
72	F	39	V	48	L	44	P	44	P	
73	S	40	A	49	V	45	L	45	L	
74	A	41	T	50	A	46	A	46	A	
75	K	42	H	51	Y	47	Y	47	Y	
76	S	43	R	52	S	48	R	48	K	
77	D	44	S	53	G	49	G	49	G	
78	L	45	K	54	P	50	L	50	L	
79	S	46	N	55	E	51	E	51	E	
80	T		-	56	N	52	T	52	T	
81	G		-	57	G	53	G	53	G	
82	N		-	58	S	54	S	54	S	
83	M		-	59	R	55	R	55	R	
84	V		-	60	E	56	E	56	E	
85	H		-	61	T	57	V	57	V	
86	A		-	62	A	58	V	58	V	
87	S	47	V	63	S	59	S	59	S	
88	Y	48	H	64	Y	60	H	60	H	
89	L	49	L	65	V	61	V	61	V	
90	L	50	Y	66	L	62	I	62	I	
91	T	51	R	67	T	63	K	63	K	
92	S	52	Q	68	N	64	Q	64	Q	
93	G	53	G	69	G	65	G	65	G	X
94	D	54	E	70	S	66	K	66	K	
95	L	55	I	71	A	67	I	67	I	
96	R	56	N	72	R	68	V	68	V	
97	F	57	L	73	F	69	F	69	F	
98	L	58	I	74	V	70	V	70	V	
99	F	59	L	75	L	71	L	71	L	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
100	T	60	N	76	T	72	S	72	C	
101	A	61	N	77	S	73	S	73	S	
102	P	62	E	78	V	74	A	74	A	
103	Y	63	P	79	I	75	L	75	L	
104	S	64	N	80	K	76	N	76	N	
105	P	65	S	81	P		-			
106	S	66	I	82	A		-			
107	L	67	A	83	T		-			
108	S	68	S	84	P	77	P	77	P	
109	A		-	85	W	78	W	78	W	
110	G		-	86	G	79	N	79	N	
111	E		-	87	H	80	K	80	K	
112	I		-	88	F	81	E	81	E	
113	K		-	89	L	82	M	82	M	
114	P		-	90	A	83	G	83	G	
115	T		-		-		-			
116	T		-		-		-			
117	T		-		-		-			
118	A		-		-		-			
119	S		-		-		-			
120	I		-		-		-			
121	P		-		-		-			
122	S		-		-		-			
123	F		-		-		-			
124	D		-		-		-			
125	H		-		-		-			
126	G		-		-		-			
127	S		-		-		-			
128	C		-		-		-			
129	R		-		-		-			
130	S	69	Y	91	D	84	D	84	D	
131	F	70	F	92	H	85	H	85	H	
132	F	71	A	93	V	86	L	86	L	
133	S	72	A	94	A	87	V	87	V	
134	S	73	E	95	E	88	K	88	K	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
135	H	74	H	96	H	89	H	89	H	X
136	G	75	G	97	G	90	G	90	G	X
137	L	76	P	98	D	91	D	91	D	
138	G	77	S	99	G	92	G	92	G	
139	V	78	V	100	V	93	V	93	V	X
140	R	79	C	101	V	94	K	94	K	
141	A	80	G	102	D	95	D	95	D	
142	V	81	M	103	L	96	I	96	I	
143	A	82	A	104	A	97	A	97	A	X
144	I	83	F	105	I	98	F	98	F	
145	E	84	R	106	E	99	E	99	E	
146	V	85	V	107	V	100	V	100	V	X
147	E	86	K	108	P	101	E	101	E	
148	D	87	D	109	D	102	D	102	D	X
149	A	88	S	110	A	103	C	103	C	
150	E	89	Q	111	R	104	D	104	E	
151	S	90	K	112	A	105	Y	105	H	
152	A	91	A	113	A	106	I	106	I	
153	F	92	Y	114	H	107	V	107	V	
154	S	93	N	115	A	108	Q	108	Q	
155	I	94	R	116	Y	109	K	109	K	
156	S	95	A	117	A	110	A	110	A	
157	V	96	L	118	I	111	R	111	R	
158	A	97	E	119	E	112	E	112	E	
159	N	98	L	120	H	113	R	113	R	
160	G	99	G	121	G	114	G	114	G	X
161	A	100	A	122	A	115	A	115	A	
162	I	101	Q	123	R	116	K	116	K	
163	P		-	124	S	117	I	117	I	
164	S		-	125	V	118	M	118	V	
165	S		-	126	A	119	R	119	R	
166	P		-	127	E	120	E	120	E	
167	P	102	P	128	P	121	P	121	P	X
168	I	103	I	129	Y	122	W	122	W	
169	V	104	H	130	E	123	V	123	V	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
170	L	105	I	131	L	124	E	124	E	
171	N	106	D	132	K	125	Q	125	E	
172	E	107	T	133	D	126	D	126	D	
173	A	108	G	134	E	127	K	127	K	
174	V	109	P	135	H	128	F	128	F	
175	T	110	M	136	G	129	G	129	G	
176	I	111	E	137	T	130	K	130	K	
177	A	112	L	138	V	131	V	131	V	
178	E	113	N	139	V	132	K	132	K	
179	V	114	L	140	L	133	F	133	F	
180	K	115	P	141	A	134	A	134	A	
181	L	116	A	142	A	135	V	135	V	
182	Y	117	I	143	I	136	L	136	L	
183	G	118	K	144	A	137	Q	137	Q	
184	D	119	G	145	T	138	T	138	T	
185	V	120	I	146	Y	139	Y	139	Y	
186	V	121	G	147	G	140	G	140	G	
187	L	122	G	148	K	141	D	141	D	
188	R	123	A	149	T	142	T	142	T	
189	Y	124	P	150	R	143	T	143	T	
190	V	125	L	151	H	144	H	144	H	
191	S	126	Y	152	T	145	T	145	T	
192	Y	127	L	153	L	146	L	146	L	
193	K	128	I	154	V	147	V	147	V	
194	A	129	D	155	D	148	E	148	E	
195	E	130	R	156	R	149	K	149	K	
196	D	131	F	157	T	150	M	150	I	
197	T	132	G	158	G	151	N	151	N	
198	E	133	E	159	Y	152	Y	152	Y	
	-	134	G		-		-			
199	K	135	S	160	D	153	I	153	T	
200	S	136	S	161	G	154	G	154	G	
201	E	137	I	162	P	155	Q	155	R	
202	F	138	Y	163	Y	156	F	156	F	
203	L	139	D	164	L	157	L	157	L	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
204	P	140	I	165	P	158	P	158	P	
205	G	141	D	166	G	159	G	159	G	
206	F	142	F	167	Y	160	Y	160	F	
207	E	143	V	168	V	161	E	161	E	
208	R	144	Y	169	A	162	A	162	A	
209	V	145	L	170	A	163	P	163	P	
210	E	146	E	171	A	164	A	164	T	
211	D	147	G		-	165	F	165	Y	
	-		-		-	166	M	166	K	
	-		-		-	167	D	167	D	
	-		-	172	P	168	P	168	T	
212	A	148	V	173	I	169	L	169	L	
213	S	149	E	174	V	170	L	170	L	
214	S	150	R	175	E	171	P	171	P	
215	F	151	N	176	P	172	K	172	K	
216	P	152	P	177	P	173	L	173	L	
217	L	153	V	178	A	174	P	174	P	
218	D	154	G	179	H	175	K	175	S	
219	Y	155	A	180	R	176	C	176	C	
220	G	156	G	181	T	177	S	177	N	
221	I	157	L	182	F	178	L	178	L	
222	R	158	K	183	Q	179	E	179	E	
223	R	159	V	184	A	180	M	180	I	
224	L	160	I	185	I	181	I	181	I	
225	D	161	D	186	D	182	D	182	D	X
226	H	162	H	187	H	183	H	183	H	X
227	A	163	L	188	C	184	I	184	I	
228	V	164	T	189	V	185	V	185	V	
229	G	165	H	190	G	186	G	186	G	
230	N	166	N	191	N	187	N	187	N	X
231	V	167	V	192	V	188	Q	188	Q	
232	P	168	Y	193	E	189	P	189	P	
	-	169	R	194	L	190	D	190	D	
	-	170	G	195	G	191	Q	191	Q	
233	E	171	R	196	R	192	E	192	E	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
234	L	172	M	197	M	193	M	193	M	
235	G	173	V	198	N	194	V	194	E	
236	P	174	Y	199	E	195	S	195	S	
237	A	175	W	200	W	196	A	196	A	
238	L	176	A	201	V	197	S	197	S	
239	T	177	N	202	G	198	E	198	E	
240	Y	178	F	203	F	199	W	199	W	
241	V	179	Y	204	Y	200	Y	200	Y	
242	A	180	E	205	N	201	L	201	L	
243	G	181	K	206	K	202	K	202	K	
244	F	182	L	207	V	203	N	203	N	
245	T	183	F	208	M	204	L	204	L	
246	G	184	N	209	G	205	Q	205	Q	
247	F	185	F	210	F	206	F	206	F	X
248	H	186	R	211	T	207	H	207	H	
249	Q	187	E	212	N	208	R	208	R	
250	F	188	A	213	M	209	F	209	F	
251	A	189	R	214	K	210	W	210	W	
252	E	190	Y	215	E	211	S	211	S	
253	F	191	F	216	F	212	V	212	V	
254	T	192	D	217	V	213	D	213	D	
255	A	193	I	218	G	214	D	214	D	
256	D	194	K	219	D	215	T	215	T	
257	D	195	G	220	D	216	Q	216	Q	
258	V	196	E	221	I	217	V	217	V	
259	G		-	222	A	218	H	218	H	
260	T		-	223	T	219	T	219	T	
261	A		-	224	E	220	E	220	E	
262	E	197	Y	225	Y	221	Y	221	Y	
263	S	198	T	226	S	222	S	222	S	
264	G	199	G	227	A	223	S	223	S	
265	L	200	L	228	L	224	L	224	L	X
266	N	201	T	229	M	225	R	225	R	
267	S	202	S	230	S	226	S	226	S	X
268	A	203	K	231	K	227	I	227	I	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
269	V	204	A	232	V	228	V	228	V	
270	L	205	M	233	V	229	V	229	V	
271	A	206	S	234	A	230	A	230	A	X
272	S	207	A	235	D	231	N	231	N	
273	N	208	P	236	G	232	Y	232	Y	
274	D	209	D	237	T	233	E	233	E	
275	E	210	G	238	L	234	E	234	E	
276	M	211	M	239	K	235	S	235	S	
277	V	212	I	240	V	236	I	236	I	
278	L	213	R	241	K	237	K	237	K	
279	L	214	I	242	F	238	M	238	M	
280	P	215	P	243	P	239	P	239	P	X
281	I	216	L	244	I	240	I	240	I	
282	N	217	N	245	N	241	N	241	N	X
283	E	218	E	246	E	242	E	242	E	X
284	P	219	E	247	P	243	P	243	P	
285	V	220	S	248	A	244	A	244	A	
286	H		-	249	L	245	P	245	P	
287	G		-	250	A	246	G	246	G	
288	T	221	S	251	K	247	K	247	R	
289	K	222	K	252	K	248	K	248	K	X
290	R	223	G		-		-			
291	K	224	A	253	K	249	K	249	K	
292	S	225	G	254	S	250	S	250	S	
293	Q	226	Q	255	Q	251	Q	251	Q	X
294	I	227	I	256	I	252	I	252	I	X
295	Q	228	E	257	D	253	Q	253	Q	
296	T	229	E	258	E	254	E	254	E	
297	Y	230	F	259	Y	255	Y	255	Y	
298	L	231	L	260	L	256	V	256	V	
299	E	232	M	261	E	257	D	257	D	
300	H	233	Q	262	F	258	Y	258	Y	
301	N	234	F	263	Y	259	N	259	N	
302	E	235	N	264	G	260	G	260	G	
303	G	236	G	265	G	261	G	261	G	X

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
304	A	237	E	266	A	262	A	262	A	
305	G	238	G	267	G	263	G	263	G	X
306	L	239	I	268	V	264	V	264	V	
307	Q	240	Q	269	Q	265	Q	265	Q	X
308	H	241	H	270	H	266	H	266	H	X
309	L	242	V	271	I	267	I	267	I	
310	A	243	A	272	A	268	A	268	A	X
311	L	244	F	273	L	269	L	269	L	
312	M	245	L	274	N	270	K	270	R	
313	S	246	T	275	T	271	T	271	T	
314	E	247	D	276	G	272	E	272	E	
315	D	248	D	277	D	273	D	273	D	X
316	I	249	L	278	I	274	I	274	I	
317	F	250	V	279	V	275	I	275	I	
318	R	251	K	280	E	276	T	276	T	
319	T	252	T	281	T	277	A	277	T	
320	L	253	W	282	V	278	I	278	I	
321	R	254	D	283	R	279	R	279	R	
322	E	255	A	284	T	280	H	280	H	
323	M	256	L	285	M	281	L	281	L	
324	R	257	K	286	R	282	R	282	R	
325	K	258	K	287	A	283	E	283	E	
326	R	259	I	288	A	284	R	284	R	
327	S		-		-		-			
328	S		-		-		-			
329	I		-		-		-			
330	G		-		-		-			
331	G	260	G	289	G	285	G	285	G	X
332	F	261	M	290	V	286	L	286	M	
333	D	262	R	291	Q	287	E	287	E	
334	F	263	F	292	F	288	F	288	F	X
335	M	264	M	293	L	289	L	289	L	
336	P	265	T	294	D	290	S	290	A	
337	S	266	A	295	T	291	V	291	V	
338	P	267	P	296	P	292	P	292	P	X

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
339	P	268	P		-		-			
340	P	269	D	297	D	293	S	293	S	
341	T	270	T	298	S	294	T	294	S	
342	Y	271	Y	299	Y	295	Y	295	Y	X
343	Y	272	Y	300	Y	296	Y	296	Y	X
344	Q	273	E	301	D	297	K	297	R	
345	N	274	M	302	T	298	Q	298	L	
346	L	275	L	303	L	299	L	299	L	X
347	K	276	E	304	G	300	R	300	R	
348	K	277	G	305	E	301	E	301	E	
349	R	278	R	306	W	302	K	302	N	
350	V	279	L	307	V	303	L	303	L	
351	G	280	P	308	G	304	K	304	K	
352	D	281	D	309	D	305	T	305	T	
353	V	282	H	310	T	306	A	306	S	
354	L	283	G	311	R	307	K	307	K	
355	S	284	E	312	V	308	I	308	I	
356	D	285	P	313	P	309	K	309	Q	
357	D	286	V	314	V	310	V	310	V	
358	Q	287	D		-	311	K	311	K	
	-	288	Q		-	312	E	312	E	
	-	289	L		-	313	N	313	N	
359	I	290	Q		-	314	I	314	M	
360	K	291	A	315	D	315	D	315	D	
361	E	292	R	316	T	316	A	316	V	
362	C	293	G	317	L	317	L	317	L	
363	E	294	I	318	R	318	E	318	E	
364	E	295	L	319	E	319	E	319	E	
365	L	296	L	320	L	320	L	320	L	X
366	G	297	D	321	K	321	K	321	K	
367	I	298	G	322	I	322	I	322	I	
368	L	299	S	323	L	323	L	323	L	
369	V	300	S	324	A	324	V	324	V	
370	D	301	V	325	D	325	D	325	D	
371	R	302	E	326	R	326	Y	326	Y	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
372	D	303	G	327	D	327	D	327	D	
373	D	304	D	328	E	328	E	328	E	
374	Q	305	K	329	D	329	K	329	K	
375	G	306	R	330	G	330	G	330	G	
376	T	307	L	331	Y	331	Y	331	Y	
377	L	308	L	332	L	332	L	332	L	X
378	L	309	L	333	L	333	L	333	L	X
379	Q	310	Q	334	Q	334	Q	334	Q	X
380	I	311	I	335	I	335	I	335	I	X
381	F	312	F	336	F	336	F	336	F	X
382	T	313	S	337	T	337	T	337	T	
383	K	314	E	338	K	338	K	338	K	
384	P	315	T	339	P	339	P	339	P	
385	L	316	L	340	V	340	V	340	M	
386	G	317	M	341	Q	341	Q	341	Q	
387	D	318	G	342	D	342	D	342	D	
388	R		-	343	R	343	R	343	R	
389	P		-	344	P	344	P	344	P	
390	T	319	P	345	T	345	T	345	T	
391	I	320	V	346	V	346	L	346	L	
392	F	321	F	347	F	347	F	347	F	X
393	I	322	F	348	F	348	L	348	L	
394	E	323	E	349	E	349	E	349	E	X
395	I	324	F	350	I	350	V	350	V	
396	I	325	I	351	I	351	I	351	I	X
397	Q	326	Q	352	E	352	Q	352	Q	
398	R	327	R	353	R	353	R	353	R	X
399	V	328	K	354	H	354	H	354	H	
400	G		-		-		-			
401	C		-		-		-			
402	M		-		-		-			
403	M		-		-		-			
404	K		-		-		-			
405	D		-		-		-			
406	E		-		-		-			

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
407	E		-		-		-			
408	G		-		-		-			
409	K		-		-		-			
410	A		-		-		-			
411	Y		-		-		-			
412	Q		-		-		-			
413	S		-		-		-			
414	G		-		-		-			
415	G	329	G	355	G	355	N	355	N	
416	C	330	D	356	S	356	H	356	H	
417	G	331	D	357	M	357	Q	357	Q	
418	G	332	G	358	G	358	G	358	G	X
419	F	333	F	359	F	359	F	359	F	X
420	G	334	G	360	G	360	G	360	G	X
421	K	335	E	361	K	361	A	361	A	
422	G	336	G	362	G	362	G	362	G	X
423	N	337	N	363	N	363	N	363	N	X
424	F	338	F	364	F	364	F	364	F	X
425	S	339	K	365	K	365	N	365	N	
426	E	340	A	366	A	366	S	366	S	
427	L	341	L	367	L	367	L	367	L	X
428	F	342	F	368	F	368	F	368	F	X
429	K	343	E	369	E	369	K	369	K	
430	S	344	S	370	A	370	A	370	A	
431	I	345	I	371	I	371	F	371	F	
432	E	346	E	372	E	372	E	372	E	X
433	E	347	R	373	R	373	E	373	E	
434	Y	348	D	374	E	374	E	374	E	
435	E	349	Q	375	Q	375	Q	375	Q	
436	K	350	V	376	E	376	N	376	A	
437	T	351	R	377	K	377	L	377	L	
438	L	352	R	378	R	378	R	378	R	
439	E	353	G	379	G	379	G	379	G	
440	A	354	V	380	N	380	N	380	N	
441	K	355	L	381	L	381	L	381	L	

(continued)

Pos.	1TFZ	Pos.	1 CJX	Pos.	1T47	Pos.	31SQ	Pos.	1SQI	Common
	A. thaliana	P. fluorescens		S. avermitilis		H. Sapiens		R. norvegicus		amino acid
442	Q	356	A			382	T	382	T	
443	L	357	T			383	N	383	D	
444	V	358	D			384	M	384	L	
445	G					385	E	385	E	
						386	T	386	T	
						387	N	387	N	
						388	G	388	G	
						389	V	389	V	
						390	V	390	R	
						391	P	391	S	
						392	G	392	G	
						393	M	393	M	
						394	A	394		
						395	E	395		
						396	N	396		
						397	L	397		
						398	Y	398		
						399	F	399		
						400	Q	400		

[0044] A sequence analysis of more than 700 HPPD sequences from public data bases including sequences of HPPD proteins and predicted HPPD proteins such as from plants, mammals, fungi and bacteria was performed using ClustalX. The alignment was corrected using the information of the available 3D structures. Identical amino acid sequences with different identifiers were included only once and some sequences with obvious sequence errors were excluded. The alignment also includes incomplete sequences. Table 2b shows the sequence alignment for a representative set of HPPD proteins and includes sequences from plants, bacteria, mammals.

Table 2b: Alignment of a representative set of HPPD sequences

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CLUSTAL X (1.81) multiple sequence alignment

RATTUS_NORVEGICUS                   ---MTT-----------------------------------YSNKGPKPE
HOMO-SAPIENS                        ---------------------------------------------GAKPE
XENOPUS-LAEVIS                      ---MTS-----------------------------------YTDKGPKPD
BLEPHARISMA-JAPONICUS               ---MTY-----------------------------------YDKQETRPD
MYCOSPHAERELLA-GRAMINICOLA          ---MAPGALLVTSQNG------------RTSPLYDSDGYVPAPAALVVGG
ASPERGILLUS-FUMIGATUS               ---MAPSAISTS----------------------------PPPTDRVSSS
MAGNAPORTHE-GRISEA                  ---MSPSAITESPRN----------------SVVDHTSGLQVDSLAVQGP
CANDIDA-ALBICANS                    --------------------------------------------------
PICHIA-STIPITIS                     ----LLKELPFLPTSS------------DPITEPDIDELLSDGHVNSKYP
RHODOCOCCUS-SP.                     ---MTIEQTLTD------------KERLAGLDLGQLEQLVGLVEYDGTRD
RHODOCOCCUS-ERYTHROPOLIS            ---MTVEQTLTD------------DEQLAGLDLEQLRQLVGLVEYDSDHD
JANIBACTER-SP.-HTCC2649             MTDTTITNPTTDTASQPTPLDLTPQEREANLNLEQLKQLVGLVEYDESKD
STREPTOMYCES-AVERMITILIS            ---MTQTTHHTP-------------------------------DTARQAD
KORDIA-ALGICIDA                     ---MAAEIKNLKD--------------------LQNTEYGLKKLFDEAED
LEEUWENHOEKIELLA-BLANDENSIS-ME      ---MSKELK--------------------------SVDYGLEKIFDGAQD
GEMMATIMONAS-AURANTIACA             ---MATLTT---------------------------------PEIGTEQD
PICROPHILUS-TORRIDUS                --------------------------------------MYGKNLISELRE
ARABIDOPSIS-THALIANA                --------MGHQNAAVSENQNHDDGAAS--SPGFKLVGFSKFVRKNPKSD
BRASSICA-RAPA-SUBSP.-PEKINENSI      --------MGHENAAVSENQHHDDAATTSASPGFKLVGFSKFVRKNPKSD
COPTIS-JAPONICA-VAR.-DISSECTA       --------------MVPST-----------ASNLKLVGHTNFVHNNPKSD
HEVEA-BRASILIENSIS                  --------MGKENDSVPSS-----------APGFKLLGFSNFVRTNPRSD
MEDICAGO-TRUNCATULA                 --------MAIETETQTQT-----------QTGFKLVGFKNFVRANPKSD
GLYCINE-MAX                         --------MCNEIQAQAQAQ---------AQPGFKLVGFKNFVRTNPKSD
SOLANUM-LYCOPERSICUM                ----MG--MGKETLS--TTDTTG--------ATFKLVGFNNFIRANPRSD
SOLANUM-TUBEROSUM                   ----MG--MGKETLSTTTTDETG--------ATFKLG-FNNFIRANPRSD
NICOTIANA-BENTHAMIANA               ----MGKLETVTTTSATAADDSSEL-----TTNFKLVGFKNFIRTNPRSD
DAUCUS-CAROTA                       ----MGKKQSEAEILSSNSSNTSP-------ATFKLVGFNNFVRANPKSD
SOLENOSTEMON-SCUTELLARIOIDES        ----MG------QESTAAAAVVP--------AEFKLVGHKNFVRSNPMSD
HORDEUM-VULGARE                     --------MPPTPTTPAAT--GAAAAVTPEHARP-----HRMVRFNPRSD
TRITICUM-AESTIVUM                   --------MPPTPTTPAATGAGAAAAVTPEHARP-----RRMVRFNPRSD
AVENA-SATIVA                        --------MPPTPATATGA---AAAAVTPEHAARS---FPRVVRVNPRSD
ORYZA-SATIVA                        --------MPPTPTPTATTGAVSAAAAAGENAGFRLVGHRRFVRANPRSD
SORGHUM-BICOLOR                     --------MPPTPTTAAAT-GAAVAAASAEQAAFRLVGHRNFVRVNPRSD
ZEA-MAYS                            --------MPPTPTAAAAG-AAVAAASAAEQAAFRLVGHRNFVRFNPRSD
AB095005_OLUCIMARINUS               --------MATVPS------------------KRKLVGCANFVRSNPLSD
OTAURI                              --------MTTSAS------------------GRKLVGHANFVRCNPLSD
MICROMONAS-PUSILLA-CCMP1545         --------MASSEANAAPA-----------AKRHKLVGCKNFVRNNPKSD
SYNECHOCOCCUS-SP.                   --------------------------------------------MNPSIR
VIBRIO-SP.-MED222                   --------------------------------------------MVDTYN
MARINOMONAS-SP.-MED121              --------------------------------------MNTALKIDYSIN
PSEUDOMONAS-FLUORESCENS             --------------------------------------------ADLYEN
SULFITOBACTER-SP.-NAS-14.1          ---------------------------------MGPFPHDAEKSKITDEN
OCEANICOLA-BATSENSIS-HTCC2597       ---------------------------------MGPFPHDAPKSEITDEN
BDELLOVIBRIO-BACTERIOVORUS          ------------------------------------------MAQVTEKN


RATTUS_NORVEGICUS                   RGRFLHFHSVTFWVGNAK--QAASFYCNKMGFEPLAYKGLETGSREVVSH
HOMO-SAPIENS                        RGRFLHFHSVTFWVGNAK--QAASFYCSKMGFEPLAYRGLETGSREVVSH
XENOPUS-LAEVIS                      VGRYLAFDHITFYVGNAK--QAAAYYATRFGFNPIAYRGLETGHRDVCTH
BLEPHARISMA-JAPONICUS               LGEFYGFHHVRFYVSNSE--QAASFYTSRFGFSPVAYEGLETGNQKFCTN
MYCOSPHAERELLA-GRAMINICOLA          EVNYRGYHHAEWWVGNAK--QVAQFYITRMGFEPVAHKGLETGSRFFASH
ASPERGILLUS-FUMIGATUS               LASYKGYDHVHWYVGNAK--QAASYYITRMGFKRIAYRGLETGCRSVCSH
MAGNAPORTHE-GRISEA                  FPSFHGYDHVTWWVGNAK--QAASYYNTLFGMKIIAYRGLETGSRYFASY
CANDIDA-ALBICANS                    ---------------------MSKYLQLAMGFKEVAYKGLETGSKLIGAH
PICHIA-STIPITIS                     TDGFIKFFSLKICSSNAK--QMSKYLQLAMDFKEIAYKGLENDSRLVGAH
RHODOCOCCUS-SP.                     PFPVSGWDAVVWVVGNAT--QTAHYFQSAFGMTLVAYSGPTTGNRDHHSF
RHODOCOCCUS-ERYTHROPOLIS            PFPVSGWDGLEWIVGNAT--QTSHFFQSAFGMELVAYSGPSTGNRDHHAF
JANIBACTER-SP.-HTCC2649             PFPVTGWDAIVFVVGNAT--QAAAYYQGTWGMELVGYSGPENGNRDHKAF
STREPTOMYCES-AVERMITILIS            PFPVKGMDAVVFAVGNAK--QAAHYYSTAFGMQLVAYSGPENGSRETASY
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KORDIA-ALGICIDA                    FLPLLGTDYVELYVGNAK--QSAHFYKTAFGFQSEAYAGLETGLTDRVSY
LEEUWENHOEKIELLA-BLANDENSIS-ME     FLPLLGTDYVEFYVGNAK--QAAHFYKTAFGFQSEAYSGLETGKKDRVSY
GEMMATIMONAS-AURANTIACA            AFPINGTDYVEFYVGNAK--QASHYYRAAFGYSLVAYRGPETGVRDRASY
PICROPHILUS-TORRIDUS               KEIFKRLHHVEFYVSSAK--TWSYFMNRGLGFKTVAYAGPETGIRDKISY
ARABIDOPSIS-THALIANA               KFKVKRFHHIEFWCGDAT--NVARRFSWGLGMRFSAKSDLSTGNMVHASY
BRASSICA-RAPA-SUBSP.-PEKINENSI     KFKVKRFHHIEFWCGDAT--NVARRFSWGLGMRFSAKSDLSTGNMVHASY
COPTIS-JAPONICA-VAR.-DISSECTA      KFHVKKFHHIEFWSTDAT--NTARRFSWGLGMPMVAKSDLSTGNMVHASY
HEVEA-BRASILIENSIS                 LFKVKRFHHVEFWCTDAT--NTACRFSWGLGMPFVAKSDLSTGNVTHASY
MEDICAGO-TRUNCATULA                RFNVKRFHHVEFWCTDAT--NTARRFSHGLGMPIVAKSDLSTGNLTHASY
GLYCINE-MAX                        RFQVNRFHHIEFWCTDAT--NASRRFSWGLGMPIVAKSDLSTGNQIHASY
SOLANUM-LYCOPERSICUM               FFSVKRFHHIEFWCGDAT--NTSRRFSWSLGMPITAKSDLSTGNSVHASY
SOLANUM-TUBEROSUM                  FFSVKRFHHIEFWCGDAT--NTSRRFSWSLGMPITAKSDLSTGNSVHASY
NICOTIANA-BENTHAMIANA              FFSVKRFHHIEFWCGDAT--NTSRRFSWSLGMPIAAKSDLSTGNSVHASY
DAUCUS-CAROTA                      HFAVKRFHHIEFWCGDAT--NTSRRFSWGLGMPLVAKSDLSTGNSVHASY
SOLENOSTEMON-SCUTELLARIOIDES       HFPVHRFHHVEFWCGDAT--NTSRRFSWGLGMPLVAKSDLSTGNSAHASY
HORDEUM-VULGARE                    RFHTLSFHHVEFWCADAA--SAAGRFAFALGAPLAARSDLSTGNSAHASQ
TRITICUM-AESTIVUM                  RFHTLSFHHVEFWCADAA--SAAGRFAFALGAPLAARSDLSTGNSVHASQ
AVENA-SATIVA                       RFPVLSFHHVELWCADAA--SAAGRFSFALGAPLAARSDLSTGNSAHASL
ORYZA-SATIVA                       RFQALAFHHVELWCADAA--SAAGRFAFALGAPLAARSDLSTGNSAHASL
SORGHUM-BICOLOR                    RFHTLAFHHVELWCADAA--SAAGRFSFGLGAPLAARSDLSTGNTAHASL
ZEA-MAYS                           RFHTLAFHHVELWCADAA--SAAGRFSFGLGAPLAARSDLSTGNSAHASL
ABO95005_OLUCIMARINUS              AFECEKFDHIEFWCGDAT--NAAARFGVGLGMGLRCKSDATTGNGTYASY
OTAURI                             AFECVGFDHVEFWCGDAT--NAASRFGVGLGMSLRAKSDASTGNGIYASY
MICROMONAS-PUSILLA-CCMP1545        LFTMRKFHHVEFWCRDAT--TTAARFAVGLGMQLVAKSDLTTGNARYASY
SYNECHOCOCCUS-SP.                  --IVQGIHHLHFYLWDLP--RWREHFCRVWGFRVASDAGN--------TL
VIBRIO-SP.-MED222                  PLGTDGFEFVEYTAVDHKGIEQLKALLVSLGFAEIAKHRSKE------AW
MARINOMONAS-SP.-MED121             PLGTDGFEFVEYTAADEKGIADLKALFVSLGFTEVAKHRSKE------VW
PSEUDOMONAS-FLUORESCENS            PMGLMGFEFIEFASPTPG---TLEPIFEIMGFTKVATHRSKN------VH
SULFITOBACTER-SP.-NAS-14.1         PAGTDGFEFVEFASADPQ---ELRDLFTRMGYAHVANHKTQK------IE
OCEANICOLA-BATSENSIS-HTCC2597      PAGTDGFEFVEFAHPDPQ---ELRDLFSKMGYELVGRHKSKD------VE
BDELLOVIBRIO-BACTERIOVORUS         PVGLNGVDFIEYSGPDAH---FFEQVFKRYAFKEVGQVHGKN------IK


RATTUS_NORVEGICUS                  VIKQGK--IVFVLCSALNPWN-----------------------------
HOMO-SAPIENS                       VIKQGK--IVFVLSSALNPWN-----------------------------
XENOPUS-LAEVIS                     VVRQNN--ATFVFQSPLNPGN-----------------------------
BLEPHARISMA-JAPONICUS              VVRSNH--VVIAFTSALTPED-----------------------------
MYCOSPHAERELLA-GRAMINICOLA         VVQNNG--VRFVFTSPVRSSA-----------------------------
ASPERGILLUS-FUMIGATUS              VVRNGD--ITFILTSPLRS-------------------------------
MAGNAPORTHE-GRISEA                 LVGKED--VRFVFTSPIRSHVH----------------------------
CANDIDA-ALBICANS                   VMQNGS--ITLEIINTLETIDDDNVLKFPFFQNDLNKFRNINHEYFLENF
PICHIA-STIPITIS                    VIRNGD--VTLEIVNTLETVEDDNVLKFPYFEKDLKQFPQLNESKYLRDF
RHODOCOCCUS-SP.                    VLESGA--VRFVIKGAVNPDSP----------------------------
RHODOCOCCUS-ERYTHROPOLIS           VLKSGA--VRFVVKGAVDPASP----------------------------
JANIBACTER-SP.-HTCC2649            VLKSGS--IRFVLKGAVSPDSP----------------------------
STREPTOMYCES-AVERMITILIS           VLTNGS--ARFVLTSVIKPATPW---------------------------
KORDIA-ALGICIDA                    VLKQDK--IRLVLTTPLGKGGE----------------------------
LEEUWENHOEKIELLA-BLANDENSIS-ME     VLRQDK--IRLVLTSPLGSASP----------------------------
GEMMATIMONAS-AURANTIACA            LMQQGK--IRLVLTTSITADTP----------------------------
PICROPHILUS-TORRIDUS               VMSQGT--ARISFTSSMNDDSY----------------------------
ARABIDOPSIS-THALIANA               LLTSGD--LRFLFTAPYSP---SLSAGEI---------------------
BRASSICA-RAPA-SUBSP.-PEKINENSI     LLTSGD--LRFLFTAPYSP---SLSAGEN---------------------
COPTIS-JAPONICA-VAR.-DISSECTA      LLRSGE--LNFLFTAPYSP---SIAGNT----------------------
HEVEA-BRASILIENSIS                 LLRSGD--LSFLFTAPYSP---TIASMENF--------------------
MEDICAGO-TRUNCATULA                LLRSGD--LNFLFSAAYSP---SISLSS----------------------
GLYCINE-MAX                        LLRSGD--LSFLFSAPYSP---SLSAGSS---------------------
SOLANUM-LYCOPERSICUM               LLRSVSGELQFVFTAPYSP---SISVPS----------------------
SOLANUM-TUBEROSUM                  LLRSVSGELQFVFTAPYSP---SISVPS----------------------
NICOTIANA-BENTHAMIANA              LLRPVSGSLQFLFTAPYSP---SISTPS----------------------
DAUCUS-CAROTA                      LVRSAN--LSFVFTAPYSP---STTTSSG---------------------
SOLENOSTEMON-SCUTELLARIOIDES       LLRSGE--LSFVFTAPYSP---SLAEPS----------------------
HORDEUM-VULGARE                    LLRSGS--LAFLFTAPYAN-----GCDAA---------------------
TRITICUM-AESTIVUM                  LLRSGN--LAFLFTAPYAN-----GCDAA---------------------
AVENA-SATIVA                       LLRSGA--LAFLFTAPYAPPPQEAATAAA---------------------
ORYZA-SATIVA                       LLRSAS--VAFLFTAPYGGDHGVGADAAT---------------------
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SORGHUM-BICOLOR                  LLRSGA--LAFLFTAPYAH-----GADAA---------------------
ZEA-MAYS                         LLRSGS--LSFLFTAPYAH-----GADAA---------------------
AB095005_OLUCIMARINUS            AMKSND--LTFVFTAPYG-----VESGGSR--------------------
OTAURI                           AMKSHD--LTFVFTAPYGDDERAVGCGGSS--------------------
MICROMONAS-PUSILLA-CCMP1545      VLQSND--LRFVFSAPYDVPEGEENDDARS--------------------
SYNECHOCOCCUS-SP.                ELEQGS--LRLRLSQPARAG------------------------------
VIBRIO-SP.-MED222                LYRQGD--INFIVNEQPHS-------------------------------
MARINOMONAS-SP.-MED121           LYRQND--INFIVNSEPNS-------------------------------
PSEUDOMONAS-FLUORESCENS          LYRQGE--INLILNNEPNS-------------------------------
SULFITOBACTER-SP.-NAS-14.1       LWQQGD--ITYVLNADPDS-------------------------------
OCEANICOLA-BATSENSIS-HTCC2597    LWQQGD--ITYIINAEPGT-------------------------------
BDELLOVIBRIO-BACTERIOVORUS       LFRQGD--INFILNCEPHT-------------------------------
                                              .

RATTUS_NORVEGICUS                --------------------------------------------------
HOMO-SAPIENS                     --------------------------------------------------
XENOPUS-LAEVIS                   --------------------------------------------------
BLEPHARISMA-JAPONICUS            --------------------------------------------------
MYCOSPHAERELLA-GRAMINICOLA       --------------------------------------------------
ASPERGILLUS-FUMIGATUS            --------------------------------------------------
MAGNAPORTHE-GRISEA               --------------------------------------------------
CANDIDA-ALBICANS                 KLTTDDLIFDFVNSRIESLSFKSDYLKFGKQFYNNIIRSDDYQESMAKVS
PICHIA-STIPITIS                  KITTNDLVFDFVNSRIESFSVSPNAHYFRRKLYNKIVSSRAFRNNMFDYN
RHODOCOCCUS-SP.                  --------------------------------------------------
RHODOCOCCUS-ERYTHROPOLIS         --------------------------------------------------
JANIBACTER-SP.-HTCC2649          --------------------------------------------------
STREPTOMYCES-AVERMITILIS         --------------------------------------------------
KORDIA-ALGICIDA                  --------------------------------------------------
LEEUWENHOEKIELLA-BLANDENSIS-ME   --------------------------------------------------
GEMMATIMONAS-AURANTIACA          --------------------------------------------------
PICROPHILUS-TORRIDUS             --------------------------------------------------
ARABIDOPSIS-THALIANA             --------------------------------------------------
BRASSICA-RAPA-SUBSP.-PEKINENSI   --------------------------------------------------
COPTIS-JAPONICA-VAR.-DISSECTA    --------------------------------------------------
HEVEA-BRASILIENSIS               --------------------------------------------------
MEDICAGO-TRUNCATULA              --------------------------------------------------
GLYCINE-MAX                      --------------------------------------------------
SOLANUM-LYCOPERSICUM             --------------------------------------------------
SOLANUM-TUBEROSUM                --------------------------------------------------
NICOTIANA-BENTHAMIANA            --------------------------------------------------
DAUCUS-CAROTA                    --------------------------------------------------
SOLENOSTEMON-SCUTELLARIOIDES     --------------------------------------------------
HORDEUM-VULGARE                  --------------------------------------------------
TRITICUM-AESTIVUM                --------------------------------------------------
AVENA-SATIVA                     --------------------------------------------------
ORYZA-SATIVA                     --------------------------------------------------
SORGHUM-BICOLOR                  --------------------------------------------------
ZEA-MAYS                         --------------------------------------------------
AB095005_OLUCIMARINUS            --------------------------------------------------
OTAURI                           --------------------------------------------------
MICROMONAS-PUSILLA-CCMP1545      --------------------------------------------------
SYNECHOCOCCUS-SP.                --------------------------------------------------
VIBRIO-SP.-MED222                --------------------------------------------------
MARINOMONAS-SP.-MED121           --------------------------------------------------
PSEUDOMONAS-FLUORESCENS          --------------------------------------------------
SULFITOBACTER-SP.-NAS-14.1       --------------------------------------------------
OCEANICOLA-BATSENSIS-HTCC2597    --------------------------------------------------
BDELLOVIBRIO-BACTERIOVORUS       --------------------------------------------------

RATTUS_NORVEGICUS                --------------------KEMGDHLVKHGDGVKDIAFEVEDCEHIVQK
HOMO-SAPIENS                     --------------------KEMGDHLVKHGDGVKDIAFEVEDCDYIVQK
XENOPUS-LAEVIS                   --------------------HPISDHVAMHGDGVKDVAFSVEDCRGIYKR
BLEPHARISMA-JAPONICUS            --------------------NEVNRHVGKHSDGVQDIAFSVSDARGMYEK
MYCOSPHAERELLA-GRAMINICOLA       -----RQTLKAAPLADQARLDEMYDHLDKHGDGVKDVAFEVDDVLAVYEN
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ASPERGILLUS-FUMIGATUS	-----LDQVDRFPPEEQELLKEIHAHLEKHGDGVKDVAFEVDSVDSVFYA
MAGNAPORTHE-GRISEA	-----LPEDEPISDEDRALLKEMHAHLEKHGDAVKDVCFEVDNVQGVYER
CANDIDA-ALBICANS	NFIVQTINNSEEIYNDMMECTLIQKFLKLHAEGVMDIAFNVNDVDTIFNR
PICHIA-STIPITIS	NLILNVINNSEVIYNDIMECTLIQKFLKTHGEGVMDISFLVEDVITIFDK
RHODOCOCCUS-SP.	----------------------LIDHHRTHGDGVVDIALAVPDVDKCIAH
RHODOCOCCUS-ERYTHROPOLIS	----------------------LIEHHSRHGDGIRDIALSVPDVDKCIAH
JANIBACTER-SP.-HTCC2649	----------------------LIAHHTKHGDGVVDISLEVPDVDKCIAQ
STREPTOMYCES-AVERMITILIS	-------------------GHFLADHVAEHGDGVVDLAIEVPDARAAHAY
KORDIA-ALGICIDA	----------------------INEHIDLHGDGVKVVALWVEDATKAFEE
LEEUWENHOEKIELLA-BLANDENSIS-ME	----------------------INEHIVKHGDGVKVVALWVEDARSAFEE
GEMMATIMONAS-AURANTIACA	----------------------IAEHVHRHGDGVRDYALWVDDARLAYET
PICROPHILUS-TORRIDUS	----------------------ISNHVKKHGDGVKDIALEVDDLDEAKSL
ARABIDOPSIS-THALIANA	-------KPTTTASIPSFDHGSCRSFFSSHGLGVRAVAIEVEDAESAFSI
BRASSICA-RAPA-SUBSP.-PEKINENSI	-------PPTTTASIPSFDHVTYRSFFSSHGLGVRAVAVEVEDAEAAFSI
COPTIS-JAPONICA-VAR.-DISSECTA	--------LTHTASIPTYSHNLARLFASTHGLAVRAIAIEVQDAELAYNI
HEVEA-BRASILIENSIS	-------SHTATASIPTFSHEACRNFSAKHGLGVRAIAIEVEDAEIAYNT
MEDICAGO-TRUNCATULA	--------PSSTAAIPTFSASTCFSFSASHGLAVRAVAVEVEDAEVAFTT
GLYCINE-MAX	--------AASSASIPSFDAATCLAFAAKHGFGVRAIALEVADAEAAFSA
SOLANUM-LYCOPERSICUM	-----------TAGIPSFSTPTYRDFTAKHGLGVRAVALEVENAYLAFSA
SOLANUM-TUBEROSUM	-----------TAGIPSFSTSTHRDFTAKHGLGVRAVALEVENAYLAFSA
NICOTIANA-BENTHAMIANA	-----------SAAIPSFSTSTHRSFAATHGLGVRAVALEVENAYTAFSA
DAUCUS-CAROTA	-----------SAAIPSFSASGFHSFAAKHGLAVRAIALEVADVAAAFEA
SOLENOSTEMON-SCUTELLARIOIDES	-----------SASIPTFSFSDHRAFTSSHGLAVRAVAIQVDSASSAYSA
HORDEUM-VULGARE	-----------TASLPSFSADAARRFSADHGIAVRSVALRVADAAEAFRA
TRITICUM-AESTIVUM	-----------TASLPSFSADAARRFSADHGLAVRSIALRVADAAEAFRA
AVENA-SATIVA	-----------TASIPSFSADAARTFAAAHGLAVRSVGVRVADAAEAFRV
ORYZA-SATIVA	-----------TASIPSFSPGAARRFAADHGLAVHAVALRVADAADAFRA
SORGHUM-BICOLOR	-----------TASLPSFSAAEARRFAADHGLAVRAVALRVADAEDAFRA
ZEA-MAYS	-----------TAALPSFSAAAARRFAADHGLAVRAVALRVADAEDAFR-
ABO95005_OLUCIMARINUS	-------GEAPHPG---HEGRAMMRFFEKHGLAARAVGVRVKDARAAYEE
OTAURI	-------VNVPHPG---NERGAMMRFFERHGLAARAVGLRVGDARAAYEE
MICROMONAS-PUSILLA-CCMP1545	-------SMFEKSGVLSHDPSFMRTFCERHGLAVRAVCLLVDDAAVAFYT
SYNECHOCOCCUS-SP.	--------------------DEVDRHLQRHGPGVVDVALAVGEQELPALA
VIBRIO-SP.-MED222	---------------------QAEAFAKVHGPSVCGMAFRVNEATAAMEQ
MARINOMONAS-SP.-MED121	---------------------QSEAFARIHGPSVCGMAFRVKDASLAMQH
PSEUDOMONAS-FLUORESCENS	---------------------IASYFAAEHGPSVCGMAFRVKDSQKAYNR
SULFITOBACTER-SP.-NAS-14.1	---------------------FAAGFVAEHGPCAPSMGWRVVDAQKALDH
OCEANICOLA-BATSENSIS-HTCC2597	---------------------HAATFIEEHGPCAPSMGWRVVDAQHAFDH
BDELLOVIBRIO-BACTERIOVORUS	---------------------FATDFAKLHGPCVNATGFRVIDADQAFKT

RATTUS_NORVEGICUS	ARERGAKIVREPWVEED------KFGKVKFAVLQTYG-DTTHTLVEK---
HOMO-SAPIENS	ARERGAKIMREPWVEQD------KFGKVKFAVLQTYG-DTTHTLVEK---
XENOPUS-LAEVIS	AIERGAKSVREPWEESD------EFGTVVMATIQTYG-DTTHTFVER---
BLEPHARISMA-JAPONICUS	AIAKGCKSFREPQVLQD------QFGSVIIASLQTYG-DTVHTLVQN---
MYCOSPHAERELLA-GRAMINICOLA	AVANGAESVSSPHTDSC------DEGDVISAAIKTYG-DTTHTFIQR---
ASPERGILLUS-FUMIGATUS	ATNNGAKIVSQPRTLED------DNGQVRVATIQTYG-ETTHTLVER---
MAGNAPORTHE-GRISEA	AVQQGAVSIAPPKTLSDK-----EHGSVTMAVIQTYG-DTTHTLLSR---
CANDIDA-ALBICANS	AIKAGSGIIRLPKIISD------ENGVVKLATISIPNSDIQHTLIEN---
PICHIA-STIPITIS	AVAAGAGIIRLPKIISD------CNGSVRLGTISIPKTDIQHTLIEN---
RHODOCOCCUS-SP.	ARAQGATVLDEPHDVTD------DHGTVRLAAIATYG-DTRHTLVDR---
RHODOCOCCUS-ERYTHROPOLIS	AITQGATVLSEPHDITD------EHGTVRLASIATYG-ETRHTLVDR---
JANIBACTER-SP.-HTCC2649	AKAAGARVVQEAETVSD------EFGSVRIGAIATYG-ETRHTLVQRTVD
STREPTOMYCES-AVERMITILIS	AIEHGARSVAEPYELKD------EHGTVVLAAIATYG-KTRHTLVDR---
KORDIA-ALGICIDA	TTKRGAKPYMEPTKEED------ENGYVIRSGIYTYG-ETVHVFVER---
LEEUWENHOEKIELLA-BLANDENSIS-ME	TTKRGAKPFMEPEVEKD------EHGEVVRSGIYTYG-ETVHMFVER---
GEMMATIMONAS-AURANTIACA	AIARGAIPIQEPQVYSD------EHGEVVIAAIGTYG-DTIHSLVER---
PICROPHILUS-TORRIDUS	IEKYGTKVS-KINEIKD------GNGKIRTAEIKTYG-ETVHTLIET---
ARABIDOPSIS-THALIANA	SVANGAIPSSPPIVLNE---------AVTIAEVKLYG-DVVLRYVSYKAE
BRASSICA-RAPA-SUBSP.-PEKINENSI	SVSNGAVPSSPPIVLND---------AVTIAEVKLYG-DVVLRYVSYKVA
COPTIS-JAPONICA-VAR.-DISSECTA	SVANGAKPSSSPIKLDE---------GVVLSEIQLYG-DVVLRYLSFKNT
HEVEA-BRASILIENSIS	SVARGALPMGGPITLDN---------RAVVAEVHLYG-DVVLRYISYKNS
MEDICAGO-TRUNCATULA	SVNLGAIPSSPPVILEN---------NVKLAEVHLYG-DVVLRYVSYNDL
GLYCINE-MAX	SVAKGAEPASPPVLVDD---------RTGFAEVRLYG-DVVLRYVSYKDA
SOLANUM-LYCOPERSICUM	SVARGAKPRFEPVTIDE---------HVAVAEVHLYG-DVVLRFVSLVKD
SOLANUM-TUBEROSUM	SVSRGAKPRFEPVTIDE---------HVAVAEVHLYG-DVVLRFVSFVKD

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NICOTIANA-BENTHAMIANA             SVSRGAKPMFEPVTIDG---------QVAMAEVHLYG-DVVLRFMS-LKD
DAUCUS-CAROTA                     SVARGARPASAPVELDD---------QAWLAEVELYG-DVVLRFVSFGRE
SOLENOSTEMON-SCUTELLARIOIDES      AVSRGAKPVSPPVVLADC--------ETAIAEVHLYG-DTVLRFVSCGSG
HORDEUM-VULGARE                   SRRRGARPAFAPVDLGR---------GFAFAEVELYG-DVVLRFVSHPDG
TRITICUM-AESTIVUM                 SVDGGARPAFSPVDLGR---------GFGFAEVELYG-DVVLRFVSHPDD
AVENA-SATIVA                      SVAGGARPAFAPADLGH---------GFGLAEVELYG-DVVLRFVSYPDE
ORYZA-SATIVA                      SVAAGARPAFQPADLGG---------GFGLAEVELYG-DVVLRFVSHPDG
SORGHUM-BICOLOR                   SVAAGARPAFEPVELGL---------GFRLAEVELYG-DVVLRYVSYPDD
ZEA-MAYS                          --------------------------GFRLAEVELYG-DVVLRYVSYPDG
ABO95005_OLUCIMARINUS             AVKRGARGVLAPTVLTHTVDDGCAKGGQVIAEIELYG-DVVLRFVNATDG
OTAURI                            AMKRGARGVLEPTEMRHEKHDGCVMGTQIISEVELYG-DVVLRFVSRADG
MICROMONAS-PUSILLA-CCMP1545       SGQHGGR-----SPAFSSACDGFAR----VSEVELYG-DVVLRYYSFHAG
SYNECHOCOCCUS-SP.                 ELLRGRG-----------------------AQLAWIP-AAAALCLHTPYG
VIBRIO-SP.-MED222                 AFKGGGEEYK-TEIGP---------MELSIPAIYGIG-ESLLYFVDRYGK
MARINOMONAS-SP.-MED121            ALANGAKEFS-GNLGA---------MELKLPAVYGIG-ESTLYFIDRYGD
PSEUDOMONAS-FLUORESCENS           ALELGAQPIH-IDTGP---------MELNLPAIKGIG-GAPLYLIDRFGE
SULFITOBACTER-SP.-NAS-14.1        AVSKGAEEYT-GAG-----------KVLDVPAIKGIG-GSLIYFVDQYYD
OCEANICOLA-BATSENSIS-HTCC2597     AVKNGATPYE-GDG-----------KVMDVPAILGIG-GSLIYFIEDYYE
BDELLOVIBRIO-BACTERIOVORUS        AVARGARPYEGNEHQK---------GATPFPAIYGIG-DSLIYFMDQKNQ

RATTUS_NORVEGICUS                 -INYTG-----RFLPGFEAPTYKDT-----LLPKLPSCNLEIIDHIVGNQ
HOMO-SAPIENS                      -MNYIG-----QFLPGYEAPAFMDP-----LLPKLPKCSLEMIDHIVGNQ
XENOPUS-LAEVIS                    -TNYKAP--AHVFLPNYRA-CEVDP-----INNVLPTVKLLNVDHVVGNQ
BLEPHARISMA-JAPONICUS             -VDYTG-----PFLPGFRAITKDDP-----LNSAFPQVNYDIIDHVVGNQ
MYCOSPHAERELLA-GRAMINICOLA        -TTYTG-----PFLPGYRSCTTVDS-----ANKFLPPVNLEAIDHCVGNQ
ASPERGILLUS-FUMIGATUS             -GSYHG-----AFLPGYRMETGVEDP----ISQLLPGVHLNRIDHCVGNQ
MAGNAPORTHE-GRISEA                -DNFRG-----TFLPGFRDVNRQPAA----YSALAP-VPLQRIDHCVGNQ
CANDIDA-ALBICANS                  -INYTG-----PFLPGFSQPIYPLADYYQVQLNMMPPVNLTVLDHCVENY
PICHIA-STIPITIS                   -IDYTG-----PFLPNYSESVTQYNSKYYDQMQNIPTVSFQCIDHCVENY
RHODOCOCCUS-SP.                   -SHYTG-----PYLPGYTARTSGHT-----KRDGAPKRLFQALDHVVGNV
RHODOCOCCUS-ERYTHROPOLIS          -SRYTG-----PYLPGYVERTSSYR-----KRDGAPKRIFQALDHVVGNV
JANIBACTER-SP.-HTCC2649           GQTYSG-----PYLPGYVARSSSFV-----KRDGAPKRLFQALDHIVGNV
STREPTOMYCES-AVERMITILIS          -TGYDG-----PYLPGYVAAAP--------IVEPPAHRTFQAIDHCVGNV
KORDIA-ALGICIDA                   -KNYNG-----VFLPGYQRWES---------HYNPEPVGLKFIDHMVGNV
LEEUWENHOEKIELLA-BLANDENSIS-ME    -KNYNG-----QFLPGYRKWES---------DYNPEPTGLKYIDHMVGNV
GEMMATIMONAS-AURANTIACA           -RNYNG-----VFLPGFKAVTP---------HYQPSDVGLKYIDHCVGNV
PICROPHILUS-TORRIDUS              -GDYNG-----VFMPGYEESEI-----------NSKNTGIKKIDHIVGNV
ARABIDOPSIS-THALIANA              DTE------KSEFLPGFERVEDASSF-------P-LDYGIRRLDHAVGNV
BRASSICA-RAPA-SUBSP.-PEKINENSI    TV----------FLPRFETVDDTSSF-------P-LDYGIRRLDHAVGNV
COPTIS-JAPONICA-VAR.-DISSECTA     N----QSCP---FLPGFEEVGEVSSS-------RGLDFGIRRLDHAVGNV
HEVEA-BRASILIENSIS                NPNLNDSSPDSWFLPKFESVDEASSF-------P-LDYGIRRLDHAVGNV
MEDICAGO-TRUNCATULA               NP---NQNPNLFFLPGFERVSDESSN-------SSLDFGIRRLDHAVGNV
GLYCINE-MAX                       APQAPHADPSRWFLPGFEAAASSSSF-------PELDYGIRRLDHAVGNV
SOLANUM-LYCOPERSICUM              ADTL-------IFLPGFEAMDETSSF-------KELDYGIHRLDHAVGNV
SOLANUM-TUBEROSUM                 EDSL-------IFLPGFEAMDETSSF-------KELDYGIRRLDHAVGNV
NICOTIANA-BENTHAMIANA             ADSL-------VFLPGFNAMDETASY-------KELDYGIRRLDHAVGNV
DAUCUS-CAROTA                     EG---------LFLPGFEAVEGTASF-------PDLDYGIRRLDHAVGNV
SOLENOSTEMON-SCUTELLARIOIDES      ADG--------WFLPGFEVVGDGVSC-------QELDYGIRRLDHAVGNV
HORDEUM-VULGARE                   TDVP--------FLPGFEGVTNP----------DAVDYGLTRFDHVVGNV
TRITICUM-AESTIVUM                 TDVP--------FLPGFEGVSNP----------DAVDYGLTRFDHVVGNV
AVENA-SATIVA                      TDLP--------FLPGFERVSSP----------GAVDYGLTRFDHVVGNV
ORYZA-SATIVA                      ADAP--------FLPGFEGVSNP----------GAVDYGLRRFDHVVGNV
SORGHUM-BICOLOR                   ADAS--------FLPGFVGVTSP----------GAADYGLRRFDHIVGNV
ZEA-MAYS                          AAGEP-------FLPGFEGVASP----------GAADYGLSRFDHIVGNV
ABO95005_OLUCIMARINUS             --------FDGDFLCNYSATRDAP----------DVSYGLQRLDHAVGNV
OTAURI                            --------FDGDFLCNYEATRDVP----------SVSYGLRRLDHAVGNV
MICROMONAS-PUSILLA-CCMP1545       EKNA----KPKTFLPGYEDVPLEPPHT------TPLTYGLQRLDHAVGNV
SYNECHOCOCCUS-SP.                 IRHS--------LIPGPLDAAPAEAG------------LFSHWDHVVLNV
VIBRIO-SP.-MED222                 -QSIYD----VDFRFYDDAEQRMAEA----------NVGLYEIDHLTHNV
MARINOMONAS-SP.-MED121            -KSIYD----VDFNFYENYQEKMLSH----------QAGLYEVDHLTHNV
PSEUDOMONAS-FLUORESCENS           GSSIYD----IDFVYLEGVERNPVG------------AGLKVIDHLTHNV
SULFITOBACTER-SP.-NAS-14.1        -TSPYN----EEYDWIAQS--KPAG------------VGFYYLDHLTHNV
OCEANICOLA-BATSENSIS-HTCC2597     -TSPYN----AEFDWLAQS--KPRG------------VGFYYLDHLTHNV
BDELLOVIBRIO-BACTERIOVORUS        -DKLYN----EIFQVKPED-KAPVG------------VGFTVVDHFTNNV
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RATTUS_NORVEGICUS	PDQEMESASEWYLKNLQFHRFWSVDDTQVHTEYSSLRSIVVANYEESIKM
HOMO-SAPIENS	PDQEMVSASEWYLKNLQFHRFWSVDDTQVHTEYSSLRSIVVANYEESIKM
XENOPUS-LAEVIS	PDDMMVPVAEWYEKMLMFHRFWSVDDTQMHTDYSALRSIVVTDYDEVIKM
BLEPHARISMA-JAPONICUS	PGGDMTPTVEWYEKYLEFHRYWSADESVIHTDYSALRSVVVADWDEVIKM
MYCOSPHAERELLA-GRAMINICOLA	DWDEMSDACDFYERCLGFHRFWSVDDKDICTEFSALKSIVMSSPNQVVKM
ASPERGILLUS-FUMIGATUS	DWDEMDKVCEYYEKALGFHRFWSVDDKQICTEYSALKSIVMASPNEVVKM
MAGNAPORTHE-GRISEA	DWDDMRAACDFYERCLSFHRFWSVDDNQISTDFSALNSIVMASPNNVVKM
CANDIDA-ALBICANS	SWNQMMEQAKLYADMFGFHKYWSVDEDDISTGFTALRSIVMSSSNGQIKM
PICHIA-STIPITIS	SWNQMMAQAKLYASLFGFHKYWSADDHDIATDNTALRSIVMASGNGKIKM
RHODOCOCCUS-SP.	ELGKMDHWVDFYNRVMGFTNMAEFVGEDIATDYSALMSKVVSNGNHRVKF
RHODOCOCCUS-ERYTHROPOLIS	ELGKMDQWVDFYNRVMGFTNMAEFVGGDIATDYSALMSKVVSSGNHRVKF
JANIBACTER-SP.-HTCC2649	ELGKMDEWVSFYNRVMGFVNMAEFVGDDIATDYSALMSKVVANGNHRVKF
STREPTOMYCES-AVERMITILIS	ELGRMNEWVGFYNKVMGFTNMKEFVGDDIATEYSALMSKVVADGTLKVKF
KORDIA-ALGICIDA	GWGEMKEWCEFYAKVMGFAQIISFTDDDISTDFTALMSKVMSNGNGRIKF
LEEUWENHOEKIELLA-BLANDENSIS-ME	GWGEMNTWVKWYEDVMGFVNFLTFDDKQITTEYSALMSKVMSNGNGRIKF
GEMMATIMONAS-AURANTIACA	ELGKMNQWVGYYADVLGFRNLITFDDTDINTEYSSLMSKVMANGNDRIKF
PICROPHILUS-TORRIDUS	YEGEMDSWVNFYIEKLGFEHLITFDDKDIRTDYSALRSKVVKY-NDDIVF
ARABIDOPSIS-THALIANA	P--ELGPALTYVAGFTGFHQFAEFTADDVGTAESGLNSAVLASNDEMVLL
BRASSICA-RAPA-SUBSP.-PEKINENSI	P--ELGPALTYLSRLTGFHQFAEFTADDVGTAESGLNSAVLANNDETVLL
COPTIS-JAPONICA-VAR.-DISSECTA	P--NLAEAIGYLKEFTGFHEFAEFTAEDVGTTESGLNSIVLASNDEMVLL
HEVEA-BRASILIENSIS	P--ELAPAVSYVKEFTGFHEFAEFTAEDVGTSESGLNSLVLANNEDTVLL
MEDICAGO-TRUNCATULA	P--ELSSAVKYVKQFTGFHEFAEFTAEDVGTSESGLNSVVLANNEETVLL
GLYCINE-MAX	P--ELAPAVRYLKGFSGFHEFAEFTAEDVGTSESGLNSVVLANNSETVLL
SOLANUM-LYCOPERSICUM	P--ELGPVVDYIKAFTGFHEFAEFTAEDVGTAESGLNSVVLANNDETVLL
SOLANUM-TUBEROSUM	P--ELGPVVDYIKEFTGFHEFAEFTAEDVGTAESGLNSVVLANNDETVLL
NICOTIANA-BENTHAMIANA	P--ELGPAVDYIKRFTGFHEFAEFTSEDVGTAESGLNSMVVANNDETVLL
DAUCUS-CAROTA	T--ELGPVVEYIKGFTGFHEFAEFTAEDVGTLESGLNSVVLANNEEMVLL
SOLENOSTEMON-SCUTELLARIOIDES	P--KLEPVVDYLKKFTGFHEFAEFTAEDVGTAESGLNSVVLANNNENVLF
HORDEUM-VULGARE	P--ELAPAAAYIAGFTGFHEFAEFTAEDVGTTESGLNSVVLANNSEGVLL
TRITICUM-AESTIVUM	P--ELAPAAAYVAGFAGFHEFAEFTTEDVGTAESGLNSMVLANNSEGVLL
AVENA-SATIVA	P--EMAPVIDYMKGFLGFHEFAEFTAEDVGTTESGLNSVVLANNSEAVLL
ORYZA-SATIVA	P--ELAPVAAYISGFTGFHEFAEFTAEDVGTAESGLNSVVLANNAETVLL
SORGHUM-BICOLOR	P--ELAPAAAYFAGFTGFHEFAEFTAEDVGTTESGLNSMVLANNAENVLL
ZEA-MAYS	P--ELAPAAAYFAGFTGFHEFAEFTTEDVGTAESGLNSMVLANNSENVLL
ABO95005_OLUCIMARINUS	H--DLIETVDYITKVTGFHEFAEFTAEDIGTIDSGLNSMVLANNNEYVLL
OTAURI	H--NLLETVDYIMKITGFHEFAEFTAEDIGTIDSGLNSMVLANNNEYVLL
MICROMONAS-PUSILLA-CCMP1545	P--NLLETVDYITAMTGMHEFAEFTAEDVGTVDSGLNSMVLANDDEMILL
SYNECHOCOCCUS-SP.	EQGSLQAAADWYGRVLGWRRLYRYS---IGTATSGLESVVVGDPEAGIQW
VIBRIO-SP.-MED222	KQGNMDVWSGFYERLGNFREIRYFDIEGKLTG---LVSRAMTSPCGKIRI
MARINOMONAS-SP.-MED121	MRGNMDHWAGFYENIGNFREIRYFDIEGKLTG---LVSRAMTSPCGKIRI
PSEUDOMONAS-FLUORESCENS	YRGRMVYWANFYEKLFNFREARYFDIKGEYTG---LTSKAMSAPDGMIRI
SULFITOBACTER-SP.-NAS-14.1	FKGNMDVWFKFYGDLFNFREIRFFDIEGKFTG---LTSRALTSPCGRIRI
OCEANICOLA-BATSENSIS-HTCC2597	FKGNMDTWFRFYGDLFNFREIRFFDIQGKYTG---LFSRALTSPCGRIRI
BDELLOVIBRIO-BACTERIOVORUS	PKGEMDKWQHFYEDIFGFYEAKYFDIRGSKTG---LLSRAMRSPCGKFSV

RATTUS_NORVEGICUS	PINEPAPGRK-KSQIQEYVDYNGGAGVQHIALRTEDIITTIRHLRER---
HOMO-SAPIENS	PINEPAPGKK-KSQIQEYVDYNGGAGVQHIALKTEDIITAIRHLRER---
XENOPUS-LAEVIS	PINEPAPGKK-KSQIQEFVEYYGGAGVQHIALRTDDILRDVSAMRAR---
BLEPHARISMA-JAPONICUS	PINEPADGLR-KSQIQEYVEYYGGAGVQHIALKVNDIISVISTLRAR---
MYCOSPHAERELLA-GRAMINICOLA	PINEPAHGKK-KSQIEEYVDFYNGPGVQHIALRTPNIIEAVSNLRSR---
ASPERGILLUS-FUMIGATUS	PINEPAKGKK-QSQIEEYVDFYNGAGVQHIALLTDDIIRDITNLKAR---
MAGNAPORTHE-GRISEA	PINEPAKGKK-RSQIEEYVTFNSGAGVQHIALLTSDIITTVEAMRSR---
CANDIDA-ALBICANS	PINEPVKSIM-KGQIEEFNDFNGGPGIQHIAFRTNNIIETVMALMQR---
PICHIA-STIPITIS	PINEPVKSKM-RGQIEEFHDFNGGPGVQHIALRTNDIIDTVCALLAR---
RHODOCOCCUS-SP.	PLNEPALAKK-RSQIDEYLDFYRGPGAQHLALATNDILTAVDQLTAE---
RHODOCOCCUS-ERYTHROPOLIS	PLNEPAIAKK-RSQIDEYLEFYQGPGAQHLALATNDILGAVDALVDE---
JANIBACTER-SP.-HTCC2649	PLNEPAIAKK-RSQIDEYLDFYQGPGAQHLAVATNDILRSVDELRKE---
STREPTOMYCES-AVERMITILIS	PINEPALAKK-KSQIDEYLEFYGGAGVQHIALNTGDIVETVRTMRAA---
KORDIA-ALGICIDA	PINEPAEGKK-KSQIEEYLDFYNGSGVQHIAVATDNIIDTVSQMRER---
LEEUWENHOEKIELLA-BLANDENSIS-ME	PINEPAEGIK-KSQIEEYLDFYEGPGVQHLAVATDDIVKTVAALKAR---
GEMMATIMONAS-AURANTIACA	PINEPASGKK-KSQIEEYLDFYGGPGAQHLALATDDILATVTALRDR---
PICROPHILUS-TORRIDUS	PINEPAKGLR-KSQIEEYLDYYRSEGVQHIALLTDDIIKTVSMMEEN---
ARABIDOPSIS-THALIANA	PINEPVHGTKRKSQIQTYLEHNEGAGLQHLALMSEDIFRTLREMRKRSS-
BRASSICA-RAPA-SUBSP.-PEKINENSI	PVNEPVHGTKRKSQIQTYLEHNEGAGVQHLALMSEDIFRTLREMRKRSG-

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COPTIS-JAPONICA-VAR.-DISSECTA      PMNEPVYGTKRKSQIQTYLEHNEGAGVQHLALVSEDIFTTLREMRRRSG-
HEVEA-BRASILIENSIS                 PLNEPVFGTKRKSQIQTYLEHNEGAGLQHLALVSEDIFKTLREMRRRSG-
MEDICAGO-TRUNCATULA                PMNEPVYGTKRKSQIETYLEHNEGAGLQHLALMSADIFRTLREMRKRSG-
GLYCINE-MAX                        PLNEPVYGTKRKSQIETYLEHNEGAGVQHLALVTHDIFTTLREMRKRSF-
SOLANUM-LYCOPERSICUM               PLNEPVYGTKRKSQIQTYLEHNEGAGVQHLALVTEDIFRTLREMWKRSG-
SOLANUM-TUBEROSUM                  PMNEPVYGTKRKSQIQTYLEHNEGAGVQHLALVTEDIFRTLREMRKRSG-
NICOTIANA-BENTHAMIANA              PLNEPVYGTKRKSQIQTYLEHNEGAGVQHLALVTEDIFKTLKEMRKRSG-
DAUCUS-CAROTA                      PLNEPVYGTKRKSQIQTYLEHNEGAGVQHLALVSEDIFRTLREMRKRSC-
SOLENOSTEMON-SCUTELLARIOIDES       PLNEPVYGTKRKSQIQTYLDHNEGAGVQHLALITEDIFRTLREMRKRSE-
HORDEUM-VULGARE                    PLNEPVHGTKRRSQIQTFLEHHGGPGVQHIAVASSDVLRTLRKMRARSA-
TRITICUM-AESTIVUM                  PLNEPVHGTKRRSQIQTFLEHHGGSGVQHIAVASSDVLRTLREMRARSA-
AVENA-SATIVA                       PLNEPVHGTKRRSQIQTYLEYHGGPGVQHIALASNDVLRTLREMRARTP-
ORYZA-SATIVA                       PLNEPVHGTKRRSQIQTYLDHHGGPGVQHIALASDDVLGTLREMRARSA-
SORGHUM-BICOLOR                    PLNEPVHGTKRRSQIQTYLDHHGGPGVQHMALASDDVLRTLREMQARSA-
ZEA-MAYS                           PLNEPVHGTKRRSQIQTFLDHHGGPGVQHMALASDDVLRTLREMQARSA-
ABO95005_OLUCIMARINUS              PVNEPTFGTKRKSQIQTYLEQNNGPGLQHLALKTDDIFATVREMRKYSHL
OTAURI                             PVNEPTFGTKRKSQIQTYLEQNNGPGLQHLALKTDDIFTTVREMRKYSHM
MICROMONAS-PUSILLA-CCMP1545        PVNEPTFGTKRKSQIQTYLECNNGAGLQHLALKSDDVFATVREMRKHGGG
SYNECHOCOCCUS-SP.                  AINEPTCAAS---QIQEFLHAHGGPGIQHAALHSSDIVASLRRLR-----
VIBRIO-SP.-MED222                  PINE-SSDDK--SQIEEFIREYNGEGIQHIALATDDIYKTVKTLRDR---
MARINOMONAS-SP.-MED121             PINE-SSDDK--SQIEEFLNQYNGEGIQHIAMSSSDIYETVRQLKAG---
PSEUDOMONAS-FLUORESCENS            PLNEESSKGA--GQIEEFLMQFNGEGIQHVAFLTDDLVKTWDALKKI---
SULFITOBACTER-SP.-NAS-14.1         PINE-DRDEK--GQIVAYLKKYNGEGIQHIAVGARNIYDATDAIADN---
OCEANICOLA-BATSENSIS-HTCC2597      PINE-DRGET--GQIVAYLKKYNGEGIQHIAVGARDIYAATDAIAEN---
BDELLOVIBRIO-BACTERIOVORUS         PINE-PTEEK--SQIQEYLDEYKGSGIQHIALLTHDINYSLESLKNS---

RATTUS_NORVEGICUS                  --GMEFLAVP-SSYYRLL--------RENLKTSK--IQVKEN-----MDV
HOMO-SAPIENS                       --GLEFLSVP-STYYKQL--------REKLKTAK--IKVKEN-----IDA
XENOPUS-LAEVIS                     --GLEFLTIP-RTYYKNL--------RARLSMSK--VQVEED-----LAE
BLEPHARISMA-JAPONICUS              --GVEFLEVP-PKYYDSL--------RKRLAHSA--VQIEED-----LKR
MYCOSPHAERELLA-GRAMINICOLA         --GVEFISVP-DTYYENM--------RLRLKAAG--MKLEES-----FDI
ASPERGILLUS-FUMIGATUS              --GVEFIKVP-DTYYEDI--------KVRLKKAG--LTLHED-----FET
MAGNAPORTHE-GRISEA                 --GVEFIEVP-HTYYDTM--------RRRLKTEKRDWELQED-----FDR
CANDIDA-ALBICANS                   --GVEFNHTS-ENYYNNL--------KQRLNNDG--IKLYED-----FDT
PICHIA-STIPITIS                    --GIEFNTAS-DKYYTNL--------ERLLREDD--VALFED-----FDT
RHODOCOCCUS-SP.                    --GVEFLATP-DSYYEDP--------ELRARIG----NVRAP-----IAE
RHODOCOCCUS-ERYTHROPOLIS           --GIEFLSTP-ASYYEDP--------ELRARIG----EVRVP-----IEE
JANIBACTER-SP.-HTCC2649            --GVEFLDTP-DAYYDDP--------EMRARIG----EVRVP-----IEE
STREPTOMYCES-AVERMITILIS           --GVQFLDTP-DSYYDT----------LGEWVG----DTRVP-----VDT
KORDIA-ALGICIDA                    --GVEFLYVP-DTYYDD----------LLERVG----DIDED-----VEE
LEEUWENHOEKIELLA-BLANDENSIS-ME     --GVEFLPPPPQAYYDD----------IPRRLGAHMDTMKED-----LNK
GEMMATIMONAS-AURANTIACA            --GVEFLSVP-TSYYED----------LQERVG----KIDEK-----LEE
PICROPHILUS-TORRIDUS               --GIEFLKTP-GSYYES----------LSSRIG----SIDED-----LNE
ARABIDOPSIS-THALIANA               IGGFDFMPSPPPTYYQN----------LKKRVG---DVLSDD----QIKE
BRASSICA-RAPA-SUBSP.-PEKINENSI     VGGFDFMPSPPPTYYKN----------LKNRVG---DVLSEE----QIEE
COPTIS-JAPONICA-VAR.-DISSECTA      VGGFEFMPSPPPTYYKN----------LKNRAG---DVLSDE----QIKE
HEVEA-BRASILIENSIS                 VGGFDFMPSPPPTYYRN----------LKNRVG---DVLTDE----QIKE
MEDICAGO-TRUNCATULA                VGGFEFMPSPPVTYYRN----------LKNRVG---DVLSDE----QIKE
GLYCINE-MAX                        LGGFEFMPSPPPTYYAN----------LHNRAA---DVLTVD----QIKQ
SOLANUM-LYCOPERSICUM               VGGFEFMPAPPPTYYKN----------LRSRAG---DVLSDE----QIQA
SOLANUM-TUBEROSUM                  VGGFEFMPSPPPTYYKN----------LKSRAG---DVLSDE----QIQA
NICOTIANA-BENTHAMIANA              VGGFEFMPSPPPTYYKN----------LKNRAG---DVLTDE----QIQA
DAUCUS-CAROTA                      LGGFEFMPSPPPTYYKN----------LKNRVG---DVLSDE----QIKE
SOLENOSTEMON-SCUTELLARIOIDES       VGGFEFMPSPPPTYYRN----------LKSRAG---DVLSDE----QIEE
HORDEUM-VULGARE                    MGGFDFLPPPLPKYYEG----------VRRLAG---DVLSEA----QIKE
TRITICUM-AESTIVUM                  MGGFDFLPPRCRKYYEG----------VRRIAG---DVLSEA----QIKE
AVENA-SATIVA                       MGGFEFMAPPQAKYYEG----------VRRIAG---DVLSEE----QIKE
ORYZA-SATIVA                       MGGFEFLAPPPPNYYDG----------VRRRAG---DVLSEE----QINE
SORGHUM-BICOLOR                    MGGFEFMAPPAPEYYDG----------VRRRAG---DVLTEA----QIKE
ZEA-MAYS                           MGGFEFMAPPTSDYYDG----------VRRRAG---DVLTEA----QIKE
ABO95005_OLUCIMARINUS              RGGFDFQAPASDDYYKQ----------LKAKIG---DALNDE----QYAL
OTAURI                             HGGFDFQAPASDDYYKH----------LKEKIG---DALTDE----QYAL
MICROMONAS-PUSILLA-CCMP1545        RGGFEFQKPASADYYAN----------LKARVGE--DALTER----QFKE
SYNECHOCOCCUS-SP.                  QGGVDFLQVAP-QYYTS----------LERELGL--ALRSALGQAISWQD
VIBRIO-SP.-MED222                  --GMDFMPTP-DTYYEKVDDRVKGHG--------------ED-----TDL
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MARINOMONAS-SP.-MED121             --GLKFMSTP-DTYYAKVNDRVVGHG--------------ED-----LEK
PSEUDOMONAS-FLUORESCENS            --GMRFMTAPPDTYYEMLEGRLPDHG--------------EP-----VDQ
SULFITOBACTER-SP.-NAS-14.1         --GLKFMPGPPETYYKMSKDRVTGHQ--------------EP-----LDR
OCEANICOLA-BATSENSIS-HTCC2597      --GVTYMPGPPDAYYDMSHDRVKDHG--------------EP-----IDR
BDELLOVIBRIO-BACTERIOVORUS         --EIQFLTPPPHSYYEMIPERVPGVT--------------ED-----ISR

RATTUS_NORVEGICUS                  LEELKILVDYD---------------EKGYLLQIFTKPMQDRPTLFLEVI
HOMO-SAPIENS                       LEELKILVDYD---------------EKGYLLQIFTKPVQDRPTLFLEVI
XENOPUS-LAEVIS                     IEKLSILVDFD---------------EEGYLLQIFTKPLEDRPTLFIEII
BLEPHARISMA-JAPONICUS              IEDLHILVDFD---------------DRGYLLQIFTKPVEDRPTLFYEII
MYCOSPHAERELLA-GRAMINICOLA         IQKLNILIDFD---------------EGGYLLQLFTKPLMDRPTVFIEII
ASPERGILLUS-FUMIGATUS              IRSLDILIDFD---------------EGGYLLQLFTKHLMDRPTVFIEII
MAGNAPORTHE-GRISEA                 LVRNNILIDYD---------------EGGYLLQLFTRPLMDRPTVFIEII
CANDIDA-ALBICANS                   LRSLNILIDYDPSTKPKPKSKRKRNNKCNYLLQIFSKPLHDRPTLFIEII
PICHIA-STIPITIS                    LRKLNILVDYDISTR------NKKTGICNYLLQIFTKPLHDRPTLFIEII
RHODOCOCCUS-SP.                    LQKRGILVDRD---------------EDGYLLQIFTKPLVDRPTVFFELI
RHODOCOCCUS-ERYTHROPOLIS           LQKRGILVDRD---------------EDGYLLQIFTKPIGDRPTVFFEII
JANIBACTER-SP.-HTCC2649            LKSRKILVDRD---------------EDGYLLQIFTKPLGDRPTVFFEII
STREPTOMYCES-AVERMITILIS           LRELKILADRD---------------EDGYLLQIFTKPVQDRPTVFFEII
KORDIA-ALGICIDA                    LKKHGILIDRD---------------EEGYLLQLFTKTIVDRPTMFFEVI
LEEUWENHOEKIELLA-BLANDENSIS-ME     LQELSILVDAD---------------EEGYLLQIFTKPLQDRPTLFFEII
GEMMATIMONAS-AURANTIACA            LAALGILVDRD---------------PDGYLLQIFTKPVEDRPTLFFEII
PICROPHILUS-TORRIDUS               IEKHNILVDRD---------------ENGYLLQIFTKPVTDRPTFFFEVI
ARABIDOPSIS-THALIANA               CEELGILVDR---------------DDQGTLLQIFTKPLGDRPTIFIEII
BRASSICA-RAPA-SUBSP.-PEKINENSI     CEELGILVDR---------------DDQGTLLQIFTKPLGDRPTIFIEII
COPTIS-JAPONICA-VAR.-DISSECTA      CEELGILVDR---------------DAQGTLLQIFTKPVGDRPTIFVEII
HEVEA-BRASILIENSIS                 CEELGILVDR---------------DDQGTLLQIFTKPVGDRPTIFIEII
MEDICAGO-TRUNCATULA                CEELGILVDR---------------DDQGTLLQIFTKPIGDRPTIFIEII
GLYCINE-MAX                        CEELGILVDR---------------DDQGTLLQIFTKPVGDRPTIFIXII
SOLANUM-LYCOPERSICUM               CEELGILVDR---------------DDQGTLLQIFTKPVGDRPTIFIEII
SOLANUM-TUBEROSUM                  CEDLGILVDR---------------DDQGTLLQIFTKPVGDRPTIFIEII
NICOTIANA-BENTHAMIANA              CEDLGILVDR---------------DDQGTLLQIFTKPVGDRPTIFIEII
DAUCUS-CAROTA                      CEDLGILVDR---------------DDQGTLLQIFTKPVGDRPTLFIEII
SOLENOSTEMON-SCUTELLARIOIDES       CEKLGILIDR---------------DDQGTLLQIFTKPVGDRPTLFIEII
HORDEUM-VULGARE                    CQELGVLVDR---------------DDQGVLLQIFTKPVGDRPTLFLEMI
TRITICUM-AESTIVUM                  CQELGVLVDR---------------DDQGVLLQIFTKPVGDRPTLFLEMI
AVENA-SATIVA                       CQELGVLVDR---------------DDQGVLLQIFTKPVGDRPTFFLEMI
ORYZA-SATIVA                       CQELGVLVDR---------------DDQGVLLQIFTKPVGDRPTFFLEMI
SORGHUM-BICOLOR                    CQELGVLVDR---------------DDQGVLLQIFTKPVGDRPTLFLEII
ZEA-MAYS                           CQELGVLVDR---------------DDQGVLLQIFTKPVGDRPTLFLEII
AB095005_OLUCIMARINUS              VEELGLLVDK---------------DDQGVLIQVFTKPVGDRPTLFLEII
OTAURI                             VEELGLLVDK---------------DDQGVLIQVFTKPVGDRPTLFLEII
MICROMONAS-PUSILLA-CCMP1545        VEELGLLVDR---------------DDQGVLVQIFTKPLGDRPTVFIEII
SYNECHOCOCCUS-SP.                  LVEQQILLDATLPASDG--------QDRPLLLQTFTQPLFGRPTFFFEVI
VIBRIO-SP.-MED222                  LRDLRVLIDGAPTKDG-------------ILLQIFTQTVIG--PVFFEII
MARINOMONAS-SP.-MED121             LQDLNILIDGAPLKDG-------------TLLQIFTDTVIG--PVFFEII
PSEUDOMONAS-FLUORESCENS            LQARGILLDGSSVEGDK-----------RLLLQIFSETLMG--PVFFEFI
SULFITOBACTER-SP.-NAS-14.1         MKKHGILIDGEGVVDGGE---------TRILLQIFSKTVIG--PIFFEFI
OCEANICOLA-BATSENSIS-HTCC2597      MKKHGILIDGEGVVDGGE---------TRILLQIFSKTVIG--PIFFEFI
BDELLOVIBRIO-BACTERIOVORUS         LEKNAILVDGD--KTG------------KYLLQIFTKNTFG--PIFYELI

RATTUS_NORVEGICUS                  QRHN---------------------HQGFGAGNFNSLFKAFEEEQALRGN
HOMO-SAPIENS                       QRHN---------------------HQGFGAGNFNSLFKAFEEEQNLRGN
XENOPUS-LAEVIS                     QRHN---------------------HQGFGAGNFKALFESIEMEQAIRGN
BLEPHARISMA-JAPONICUS              QRHN---------------------NNGFGIGNFKALFESLEQEQERRGN
MYCOSPHAERELLA-GRAMINICOLA         QRNN---------------------FDGFGAGNFKSLFEAIEREQDLRGN
ASPERGILLUS-FUMIGATUS              QRHN---------------------FSGFGAGNFKSLFEAIEREQALRGN
MAGNAPORTHE-GRISEA                 QRNE---------------------FDGFGAGNFKSLFEAIEREQAERGN
CANDIDA-ALBICANS                   QRHH---------------------HNGFGKGTFKGLFESIEEQQKLRGT
PICHIA-STIPITIS                    QRHH---------------------HNGFGKGTFKGLFETIEEQQRIRGT
RHODOCOCCUS-SP.                    ERHG---------------------SLGFGIGNFKALFEAIEREQAARGN
RHODOCOCCUS-ERYTHROPOLIS           ERHG---------------------SLGFGLGNFKALFEAIEREQAARGN
JANIBACTER-SP.-HTCC2649            ERHG---------------------SLGFGKGNFKALFESIEREQDARGN
STREPTOMYCES-AVERMITILIS           ERHG---------------------SMGFGKGNFKALFEAIEREQEKRGN
KORDIA-ALGICIDA                    QRKG---------------------AQSFGVGNFKALFEAIEREQAARGT
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LEEUWENHOEKIELLA-BLANDENSIS-ME   QRMG---------------------AKGFGAGNFKALFESIEREQAQRGT
GEMMATIMONAS-AURANTIACA          QRKG---------------------ATSFGKGNFRALFEAIEREQELRGN
PICROPHILUS-TORRIDUS             QRKG---------------------ARSFGNGNFKALFEAIEREQAKRGN
ARABIDOPSIS-THALIANA             QRVGCMMKDEEGKA------YQSGGCGGFGKGNFSELFKSIEEYEKTLEA
BRASSICA-RAPA-SUBSP.-PEKINENSI   QRIGCMKKDEEGRV------YQSGGCGGFGKGNFSELFKSIEEYEKTLEA
COPTIS-JAPONICA-VAR.-DISSECTA    QRLGCMLKDEEGKT------YQKAGCGGFGKGNFSELFKSIEEYEKTLEA
HEVEA-BRASILIENSIS               QRVGCMIKDETGKE------YQKGGCGGFGKGNFSELFKSIEEYEKTLEA
MEDICAGO-TRUNCATULA              QRVGCMLKDEEGKE------YQKGGCGGFGKGNFSELFKSIEEYEKTLET
GLYCINE-MAX                      QRIGCMVEDEEGKV------YQKGACGGFGKGNFSELFKSIEEYEKTLEA
SOLANUM-LYCOPERSICUM             QRIGCMLKDEKGQV------YQKGGCGGFGKGNFSELFRSIEEYEKMLEA
SOLANUM-TUBEROSUM                QRIGCMLKDENGQV------YQKGGCGGFGKGNFSELFRSIEEYEKMLEA
NICOTIANA-BENTHAMIANA            QRIGCMLKDEKGQV------YQKGGCGGFGKGNFWELFRSIEEYEKTL--
DAUCUS-CAROTA                    QRVGCMLKDDAGQM------YQKGGCGGFGKGNFSELFKSIEEYEKTLEA
SOLENOSTEMON-SCUTELLARIOIDES     QRVGCMMKDEEGKM------YQKGGCGGFGKGNFSELFKSIEEYEKMLES
HORDEUM-VULGARE                  QRIGCMEKDERGEE------YQKGGCGGFGKGNFSELFKSIEDYEKSLEA
TRITICUM-AESTIVUM                QRIGCMEKDERGEE------YQKGGCGGFGKGNFSELFKSIEDYEKSLEA
AVENA-SATIVA                     QRIGCMEKDEVGQE------YQKGGCGGFGKGNFSELFKSIEDYEKSLEV
ORYZA-SATIVA                     QRIGCMEKDESGQE------YQKGGCGGFGKGNFSELFKSIEEYEKSLEA
SORGHUM-BICOLOR                  QRIGCMEKDEKGQE------YQKGGCGGFGKGNFSQLFKSIEDYEKSLEA
ZEA-MAYS                         QRIGCMEKDEKGQE------YQKGGCGGFGKGNFSQLFKSIEDYEKSLEA
AB095005_OLUCIMARINUS            QRIGCMRRKADSES-----FEQAAGCGGFGKGNFSELFKSIEAYEATLQI
OTAURI                           QRVGCMRKKADTDE-----LEQVAGCGGFGKGNFSELFKSIEAYEKTLNI
MICROMONAS-PUSILLA-CCMP1545      QRIGCLREVKSADANAPPRIEQAGGCGGFGKGNFSELFKSIENYERTLKM
SYNECHOCOCCUS-SP.                QRLG--------------------GATGFGEANFQALFEALERQQRQRHQ
VIBRIO-SP.-MED222                QRKG---------------------NEGFGEGNFKALFESIEEDQIRRGV
MARINOMONAS-SP.-MED121           QRKG---------------------NEGFGEGNFKALFESIEEDQIRRGV
PSEUDOMONAS-FLUORESCENS          QRKG---------------------DDGFGEGNFKALFESIERDQVRRGV
SULFITOBACTER-SP.-NAS-14.1       ERKG---------------------DDGFGEGNFKALFESIEQEQIDSGE
OCEANICOLA-BATSENSIS-HTCC2597    QRKG---------------------DDGFGEGNFKALFESIEQEQIDNGE
BDELLOVIBRIO-BACTERIOVORUS       QRKG---------------------HDGFGDGNFQALFDAIERDQRERGY


RATTUS_NORVEGICUS                LTDLETNGVRSGM-------
HOMO-SAPIENS                     LTNMETNGVVPGMAENLYFQ
XENOPUS-LAEVIS                   L-------------------
BLEPHARISMA-JAPONICUS            LI------------------
MYCOSPHAERELLA-GRAMINICOLA       L-------------------
ASPERGILLUS-FUMIGATUS            LV------------------
MAGNAPORTHE-GRISEA               L-------------------
CANDIDA-ALBICANS                 FVKSQNN-------------
PICHIA-STIPITIS                  LVQVDEDDDSQQST------
RHODOCOCCUS-SP.                  F-------------------
RHODOCOCCUS-ERYTHROPOLIS         F-------------------
JANIBACTER-SP.-HTCC2649          L-------------------
STREPTOMYCES-AVERMITILIS         L-------------------
KORDIA-ALGICIDA                  L-------------------
LEEUWENHOEKIELLA-BLANDENSIS-ME   L-------------------
GEMMATIMONAS-AURANTIACA          L-------------------
PICROPHILUS-TORRIDUS             L-------------------
ARABIDOPSIS-THALIANA             KQLVG---------------
BRASSICA-RAPA-SUBSP.-PEKINENSI   KQLVG---------------
COPTIS-JAPONICA-VAR.-DISSECTA    KANVVAA-------------
HEVEA-BRASILIENSIS               KRNAEAR-------------
MEDICAGO-TRUNCATULA              RRTA----------------
GLYCINE-MAX                      KRTA----------------
SOLANUM-LYCOPERSICUM             KHVNQVAAVE----------
SOLANUM-TUBEROSUM                KHVNQVAAA-----------
NICOTIANA-BENTHAMIANA            --------------------
DAUCUS-CAROTA                    KQITGSAAA-----------
SOLENOSTEMON-SCUTELLARIOIDES     KLVTKTAMA-----------
HORDEUM-VULGARE                  KQSAAVQGS-----------
TRITICUM-AESTIVUM                KQSAAVQGS-----------
AVENA-SATIVA                     KQSVVAQKS-----------
ORYZA-SATIVA                     KQAPTVQGS-----------
SORGHUM-BICOLOR                  KQAAAAQGS-----------
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ZEA-MAYS	KQAAAAAAAQGS--------
ABO95005_OLUCIMARINUS	--------------------
OTAURI	--------------------
MICROMONAS-PUSILLA-CCMP1545	--------------------
SYNECHOCOCCUS-SP.	ALTP----------------
VIBRIO-SP.-MED222	LDDA----------------
MARINOMONAS-SP.-MED121	LNDA----------------
PSEUDOMONAS-FLUORESCENS	LATD----------------
SULFITOBACTER-SP.-NAS-14.1	LSEA----------------
OCEANICOLA-BATSENSIS-HTCC2597	IAAE----------------
BDELLOVIBRIO-BACTERIOVORUS	LT------------------

[0045] The overall sequence identity between individual full length HPPD sequences is in general quite low and is shown for the representative HHPD proteins in Table 3. Table 4a shows the sequence alignment of the binding pocket. In contrast, the sequence identity of the 36 amino acids forming the binding site is significantly higher which is shown for the representative HPPD proteins in Table 4b. In particular, the amino acids at 8 positions are strictly conserved in all species and illustrate that these amino acids have a key role (e.g. His226, His308, Glu394 binding the iron required for catalysis). These positions, with reference to the HPPD from Arabidopsis (SEQ ID No. 2) are His226, Ser267, Asn282, His308, Tyr342, Glu394, Gly420, Asn423 (Table 5a). A mutation of any of the amino acids at either of these positions will most likely lead to an inactive protein. The variability at other positions within the binding site is higher. Table 5b shows the 28 variable positions in the binding site and the amino acids which were identified at these positions using the sequence alignment. Some positions have only limited variability which reflects their role in the 3D environment. An example for this represents the position 269. All HPPD proteins have at this position either a Val, Ala or Thr. Looking at the 3D structures it seems that at this position a small apolar amino acid is required and a mutation to a polar amino acid such as Arg, His or Lys will disturb the protein structure locally. Another example represents position 379. Most sequences have a glutamine at position 379. However, there are also some bacterial sequences which have a histidine at this position. Looking at the 3D structure, it seems that only few amino acids are tolerated at this position. Gln379 in *A.thaliana* stabilizes via its H-bond donor the side chain conformation of the strictly conserved Glu394 which in turn interacts with the catalytic iron. In addition, with its H-bond acceptors Gln379 stabilizes the side chain conformation of the strictly conserved Asn423 which in turn interacts with the strictly conserved Tyr342. Only glutamine, asparagine and histidine have an H-bond donor and acceptor required for the stabilization of this particular 3D arrangement which very likely play a key role in the interaction of the C-terminal helix with the core of the HPPD protein. Limited variability is also seen at position 381 with either a phenylalanine or a tyrosine in all HPPD sequences. The aromatic ring stabilizes the binding of HPPD inhibitors and very likely also the binding of the substrate to the HPPD binding. However, the presence of the additional hydroxyl group in tyrosine compared to phenylalanine does not disturb the catalytic activity. The third category of positions includes those positions which display a very high natural variability. These positions may not be crucial for substrate binding and catalysis but influence inhibitor binding. These positions include adjacent positions in strand 248 to 255 and positions in the C-terminal helix 419-427. It can be assumed that the interaction of this particular strand and the C-terminal helix with the core of the protein plays a crucial role in inhibitor binding. Table 5b includes for each variable position those amino acids which have been identified in the sequence alignments using all known HPPD sequences.

Table 3: Pairwise sequence identity of HPPD sequences from the representative set of HPPD proteins

RATTUS_NORVEGICUS	100	90	62	55	52	53	50	44	41	42	39	41	45	45	48	48	45	37	37	36	36	37	37	36	36	36	36	37	35	35	35	35	36	35	34	34	32	31	29	28	27	24	24	30
HOMO-SAPIENS	90	100	63	55	53	55	51	42	41	42	40	42	46	46	49	48	45	36	37	37	37	37	38	37	37	38	37	37	35	35	35	35	35	35	34	35	34	31	29	29	27	25	25	31
XENOPUS-LAEVIS	62	63	100	60	54	57	52	44	44	43	42	43	49	48	51	49	45	37	37	36	34	34	34	38	38	38	38	37	36	36	36	36	35	36	36	36	35	30	31	32	31	28	25	31
BLEPHARISMA-JAPONICUS	55	55	60	100	49	49	47	41	40	42	41	41	45	42	46	48	45	35	35	35	35	34	36	35	35	35	36	36	35	34	36	35	35	34	34	34	32	31	30	31	26	26	26	29
MYCOSPHAERELLA-GRAMINICOLA	52	53	54	49	100	65	61	45	40	44	43	41	46	48	47	48	44	34	34	34	32	32	33	34	33	33	33	34	31	30	32	32	32	31	33	33	31	30	33	34	32	29	28	32
ASPERGILLUS-FUMIGATUS	53	55	57	49	65	100	63	45	43	43	42	44	46	49	51	49	46	33	33	32	31	32	32	33	33	33	34	35	32	31	32	32	33	32	32	33	30	29	35	34	32	27	28	33
MAGNAPORTHE-GRISEA	50	51	52	47	61	63	100	42	40	41	40	40	46	45	45	47	41	33	34	34	32	32	32	33	33	34	33	35	32	31	33	32	32	32	34	33	33	30	33	30	29	26	26	31
CANDIDA-ALBICANS	44	42	44	41	45	45	42	100	66	37	37	37	38	41	41	43	38	28	28	28	27	29	28	28	28	29	28	28	28	28	27	28	28	29	26	26	26	27	33	32	33	28	30	31
PICHIA-STIPITIS	41	41	44	40	40	43	40	66	100	36	36	36	37	37	38	39	38	26	26	28	25	27	26	26	25	27	26	26	26	26	26	26	27	26	25	24	25	26	32	29	30	25	26	32
RHODOCOCCUS-SP.	42	42	43	42	44	43	41	37	36	100	85	77	62	48	49	55	46	34	34	36	35	35	36	36	35	35	36	38	35	34	37	36	37	36	36	36	34	34	30	31	32	29	29	32
RHODOCOCCUS-ERYTHROPOLIS	39	40	42	41	43	42	40	37	36	85	100	75	60	47	49	55	46	35	35	36	34	36	36	36	36	35	37	39	34	33	36	34	36	35	35	35	34	32	30	30	31	30	29	31
JANIBACTER-SP.-HTCC2649	41	42	43	41	41	44	40	37	36	77	75	100	63	47	49	53	44	34	35	34	34	34	36	36	35	35	35	37	32	32	33	33	34	34	36	36	33	32	31	30	31	29	29	32
STREPTOMYCES-AVERMITILIS	45	46	49	45	46	46	46	38	37	62	60	63	100	50	53	58	46	38	38	38	37	37	38	37	37	37	38	39	35	34	35	35	36	36	38	38	35	34	34	33	32	32	30	33
KORDIA-ALGICIDA	45	46	48	42	48	49	45	41	37	48	47	47	50	100	73	60	53	35	35	34	32	34	32	34	35	34	34	36	34	34	34	35	34	34	34	35	34	31	37	35	34	33	34	35
LEEUWENHOEKIELLA-BLANDENSIS-ME	48	49	51	46	47	51	45	41	38	49	49	49	53	73	100	63	51	38	38	36	36	37	37	39	38	38	37	39	38	37	37	38	38	39	38	38	36	34	37	38	36	32	33	36
GEMMATIMONAS-AURANTIACA	48	48	49	48	48	49	47	43	39	55	55	53	58	60	63	100	53	39	39	39	39	39	39	39	39	38	40	43	39	37	38	38	39	39	40	40	38	36	37	35	35	34	33	36
PICROPHILUS-TORRIDUS	45	45	45	45	44	46	41	38	38	46	46	44	46	53	51	53	100	35	35	35	36	35	35	35	36	36	36	37	32	32	32	33	33	34	32	33	33	33	33	33	33	29	29	34
ARABIDOPSIS-THALIANA	37	36	37	35	34	33	33	28	26	34	35	34	38	35	38	39	35	100	90	75	76	75	73	72	72	70	73	71	60	60	61	61	63	63	55	56	57	31	28	29	25	27	27	30
BRASSICA-RAPA-SUBSP.-PEKINENSI	37	37	37	35	34	33	34	28	26	34	35	35	38	35	38	39	35	90	100	75	76	76	75	74	74	73	73	72	60	60	61	61	62	63	57	57	58	31	28	28	26	27	27	29
COPTIS-JAPONICA-VAR.-DISSECTA	36	37	36	35	34	32	34	28	28	36	36	34	38	34	36	39	35	75	75	100	78	74	71	73	73	72	73	72	61	61	62	62	64	64	55	56	58	29	29	31	29	28	28	31
HEVEA-BRASILIENSIS	36	37	34	35	32	31	32	27	25	35	34	34	37	32	36	39	36	76	76	78	100	78	74	75	75	74	74	72	62	62	62	63	64	64	56	57	57	29	28	29	27	27	27	30
MEDICAGO-TRUNCATULA	37	37	34	34	32	32	32	29	27	35	36	34	37	34	37	39	35	75	76	74	78	100	76	74	75	74	75	74	62	62	63	63	65	65	55	56	59	29	29	30	27	27	27	29
GLYCINE-MAX	37	38	34	36	33	32	32	28	26	36	36	36	38	32	37	39	35	73	75	71	74	76	100	75	74	74	75	73	62	62	62	63	66	67	54	55	56	29	30	30	26	27	26	31
SOLANUM-LYCOPERSICUM	36	37	38	35	34	33	33	28	26	36	36	36	37	34	39	39	35	72	74	73	75	74	75	100	96	87	77	76	63	62	62	65	64	64	56	57	57	30	28	29	26	27	26	30
SOLANUM-TUBEROSUM	36	37	38	35	33	33	33	28	25	35	36	35	37	35	38	39	36	72	74	73	75	75	74	96	100	88	78	76	62	61	62	64	62	63	56	57	57	30	29	29	26	27	26	30
NICOTIANA-BENTHAMIANA	36	38	38	35	33	33	34	29	27	35	35	35	37	34	38	38	36	70	73	72	74	74	74	87	88	100	76	75	61	60	61	63	64	64	55	56	56	31	31	30	27	27	26	30
DAUCUS-CAROTA	36	37	38	36	33	34	33	28	26	36	37	35	38	34	37	40	36	73	73	73	74	75	75	77	78	76	100	76	63	62	64	65	65	65	58	59	59	29	29	30	27	27	26	29
SOLENOSTEMON-SCUTELLARIOIDES	37	37	37	36	34	35	35	28	26	38	39	37	39	36	39	43	37	71	72	72	72	74	73	76	76	75	76	100	62	60	62	64	64	65	58	59	57	30	30	31	27	28	27	30
HORDEUM-VULGARE	35	35	36	35	31	32	32	28	26	35	34	32	35	34	38	39	32	60	60	61	62	62	62	63	62	61	63	62	100	95	83	83	83	83	54	55	54	33	30	30	27	27	28	30
TRITICUM-AESTIVUM	35	35	36	34	30	31	31	28	26	34	33	32	34	34	37	37	32	60	60	61	62	62	62	62	61	60	62	60	95	100	83	82	82	82	53	54	54	32	30	30	26	28	28	30
AVENA-SATIVA	35	35	36	36	32	32	33	27	26	37	36	33	35	34	37	38	32	61	61	62	62	63	62	62	62	61	64	62	83	83	100	81	80	79	54	53	54	30	30	29	27	27	28	31
ORYZA-SATIVA	35	35	36	35	32	32	32	28	26	36	34	33	35	35	38	38	33	61	61	62	63	63	63	65	64	63	65	64	83	82	81	100	84	83	54	56	55	32	29	29	27	26	28	31
SORGHUM-BICOLOR	36	35	35	35	32	33	32	28	27	37	36	34	36	34	38	39	33	63	62	64	64	65	66	64	62	64	65	64	83	82	80	84	100	93	54	56	56	30	29	30	27	26	27	29
ZEA-MAYS	35	35	36	34	31	32	32	29	26	36	35	34	36	34	39	39	34	63	63	64	64	65	67	64	63	64	65	65	83	82	79	83	93	100	55	57	57	32	30	31	27	26	26	29
AB095005_OLUCIMARINUS	34	34	36	34	33	32	34	26	25	36	35	36	38	34	38	40	32	55	57	55	56	55	54	56	56	55	58	58	54	53	54	54	54	55	100	84	63	28	30	27	25	25	27	27
OTAURI	34	35	36	34	33	33	33	26	24	36	35	36	38	35	38	40	33	56	57	56	57	56	55	57	57	56	59	59	55	54	53	56	56	57	84	100	62	28	31	29	25	26	27	27
MICROMONAS-PUSILLA-CCMP1545	32	34	35	32	31	30	33	26	25	34	34	33	35	34	36	38	33	57	58	58	57	59	56	57	57	56	59	57	54	54	54	55	56	57	63	62	100	29	27	28	24	25	25	27
SYNECHOCOCCUS-SP.	31	31	30	31	30	29	30	27	26	34	32	32	34	31	34	36	33	31	31	29	29	29	29	30	30	31	29	30	33	32	30	32	30	32	28	28	29	100	26	27	28	23	24	28
VIBRIO-SP.-MED222	29	29	31	30	33	35	33	33	32	30	30	31	34	37	37	37	33	28	28	29	28	29	30	28	29	31	29	30	30	30	30	29	29	30	30	31	27	26	100	74	53	53	50	46
MARINOMONAS-SP.-MED121	28	29	32	31	34	34	30	32	29	31	30	30	33	35	38	35	33	29	28	31	29	30	30	29	29	30	30	31	30	30	29	29	30	31	27	29	28	27	74	100	56	51	49	44
PSEDUMONOASE-FLUORESCENCE	27	27	31	26	32	32	29	33	30	32	31	31	32	34	36	35	33	25	26	29	27	27	26	26	26	27	27	27	27	26	27	27	27	27	25	25	24	28	53	56	100	48	50	43
SULFITOBACTER-SP.-NAS-14.1	24	25	28	26	29	27	26	28	25	29	30	29	32	33	32	34	29	27	27	28	27	27	27	27	27	27	27	28	27	28	27	26	26	26	25	26	25	23	53	51	48	100	81	45
OCEANICOLA-BATSENSIS-HTCC2597	24	25	25	26	28	28	26	30	26	29	29	29	30	34	33	33	29	27	27	28	27	27	26	26	26	26	26	27	28	28	28	28	27	26	27	27	25	24	50	49	50	81	100	45
BDELLOVIBRIO-BACTERIOVORUS	30	31	31	29	32	33	31	31	32	32	31	32	33	35	36	36	34	30	29	31	30	29	31	30	30	30	29	30	30	30	31	31	29	29	27	27	27	28	46	44	43	45	45	100

Table 4a: Sequence alignment of amino acids forming the binding pocket in the representative set of HPPD sequences

HOMO-SAPIENS	HVHFWSVLSIVVAPNQIQHLYLQFFEFGAGNFNSLF
RATTUS_NORVEGICUS	HVHFWSVLSIVVAPNQIQHLYLQFFEFGAGNFNSLF
XENOPUS-LAEVIS	HVHFWSVLSIVVTPNQIQHLYLQFFEFGAGNFKALI
ASPERGILLUS-FUMIGATUS	HVHFWSVLSIVMAPNQIQHIYLQFFEFGAGNFKSLI
MAGNAPORTHE-GRISEA	HVHFWSVLSIVMAPNQIQHIYLQFFEFGAGNFKSLI
MYCOSPHAERELLA-GRAMINICOLA	HVHFWSVLSIVMSPNQIQHIYLQFFEFGAGNFKSLI
CANDIDA-ALBICANS	HVHYWSVLSIVMSPNQIQHNYLQFFEFGKGTFKGLI
PICHIA-STIPITIS	HVHYWSALSIVMAPNQIQHNYLQFFEFGKGTFKGLI
ARABIDOPSIS-THALIANA	HVHFAEFLSAVLAPNQIQHMYLQFFEFGKGNFSELI
BRASSICA-RAPA-SUBSP.-PEKINENSI	HVHFAEFLSAVLAPNQIQHMYLQFFEFGKGNFSELI
HEVEA-BRASILIENSIS	HVHFAEFLSLVLAPNQIQHMYLQFFEFGKGNFSELI
COPTIS-JAPONICA-VAR.-DISSECTA	HVHFAEFLSIVLAPNQIQHMYLQFFEFGKGNFSELI
SOLENOSTEMON-SCUTELLARIOIDES	HVHFAEFLSVVLAPNQIQHMYLQFFEFGKGNFSELI
AVENA-SATIVA	HVHFAEFLSVVLAPNQIQHMYLQFFEFGKGNFSELI
DAUCUS-CAROTA	HVHFAEFLSVVLAPNQIQHMYLQFFEFGKGNFSELI
SOLANUM-TUBEROSUM	HVHFAEFLSVVLAPNQIQHMYLQFFEFGKGNFSELI
SOLANUM-LYCOPERSICUM	HVHFAEFLSVVLAPNQIQHMYLQFFEFGKGNFSELI
MEDICAGO-TRUNCATULA	HVHFAEFLSVVLAPNQIQHMYLQFFEFGKGNFSELI
GLYCINE-MAX	HVHFAEFLSVVLAPNQIQHMYLQFFXFGKGNFSELI
HORDEUM-VULGARE	HVHFAEFLSVVLAPNQIQHLYLQFFEFGKGNFSELI
ORYZA-SATIVA	HVHFAEFLSVVLAPNQIQHLYLQFFEFGKGNFSELI
SORGHUM-BICOLOR	HVHFAEFLSMVLAPNQIQHMYLQFFEFGKGNFSQLI
ZEA-MAYS	HVHFAEFLSMVLAPNQIQHMYLQFFEFGKGNFSQLI
AB095005_OLUCIMARINUS	HVHFAEFLSMVLAPNQIQHQYLQFFEFGKGNFSELI

(continued)

OTAURI	HVHFAEFLSMVLAPNQIQHQYLQFFEFGKGNFSELI
MICROMONAS-PUSILLA-CCMP1545	HVHFAEFLSMVLAPNQIQHQYLQFFEFGKGNFSELI
TRITICUM-AESTIVUM	HVHFAEFLSMVLAPNQIQHLYLQFFEFGKGNFSELI
NICOTIANA-BENTHAMIANA	HVHFAEFLSMVVAPNQIQHMYLQFFEFGKGNFWELI
RHODOCOCCUS-SP.	HVTMAEFLSKVVSPNQIQHLYLQFFEFGIGNFKALI
RHODOCOCCUS-ERYTHROPOLIS	HVTMAEFLSKVVSPNQIQHLYLQFFEFGLGNFKALI
STREPTOMYCES-AVERMITILIS	HVTMKEFLSKVVAPNQIQHLYLQFFEFGKGNFKALI
JANIBACTER-SP.-HTCC2649	HVVMAEFLSKVVAPNQIQHLYLQFFEFGKGNFKALI
KORDIA-ALGICIDA	HVAIISFLSKVMSPNQIQHLYLQFFEFGVGNFKALI
LEEUWENHOEKIELLA-BLANDENSIS-ME	HVVFLTFLSKVMSPNQIQHLYLQFFEFGAGNFKALI
PICROPHILUS-TORRIDUS	HVELITFLSKVVKPNQIQHLYLQFFEFGNGNFKALI
GEMMATIMONAS-AURANTIACA	HVRLITFLSKVMAPNQIQHLYLQFFEFGKGNFRALI
VIBRIO-SP.-MED222	HTRIRYFLSRAMTPNQIQHMYLQFFEFGEGNFKALI
MARINOMONAS-SP.-MED121	HTRIRYFLSRAMTPNQIQHMYLQFFEFGEGNFKALI
SULFITOBACTER-SP.-NAS-14.1	HTRIRFFLSRALTPNQIQHMYLQFFEFGEGNFKALI
OCEANICOLA-BATSENSIS-HTCC2597	HTRIRFFLSRALTPNQIQHMYLQFFEFGEGNFKALI
PSEUDOMONAS-FLUORESCENS	HTRARYFLSKAMSPNQIQHMYLQFFEFGEGNFKALI
BDELLOVIBRIO-BACTERIOVORUS	HTYAKYFLSRAMRPNQIQHLYLQFFEFGDGNFQALI
BLEPHARISMA-JAPONICUS	HVHYWSALSWVAPNQIQHLYLQFFEFGIGNFKALL
SYNECHOCOCCUS-SP.	HVRLYRYLSVVVGANQIQHLYLQFFEFGEANFQALL

Table 4b: Pairwise sequence identity of amino acids forming the binding site HPPD in the representative set

HOMO-SAPIENS	100	100	89	89	89	86	75	75	72	72	72	75	72	72	72	72	72	72	69	75	75	72	72	72	72	72	75	75	69	69	72	72	69	72	69	69	58	58	58	58	58	61	81	64
RATTUS_NORVEGICUS	100	100	89	89	89	86	75	75	72	72	72	75	72	72	72	72	72	72	69	75	75	72	72	72	72	72	75	75	69	69	72	72	69	72	69	69	58	58	58	58	58	61	81	64
XENOPUS-LAEVIS	89	89	100	89	89	89	81	78	72	72	72	75	72	72	72	72	72	72	69	75	75	72	72	72	72	72	75	75	78	78	78	78	78	81	78	72	69	69	69	69	67	67	83	67
ASPERGILLUS-FUMIGATUS	89	89	89	100	100	97	83	83	75	75	75	78	75	75	75	75	75	75	72	75	75	75	75	75	75	75	75	75	69	69	72	72	75	78	69	72	67	67	64	64	67	64	78	58
MAGNAPORTHE-GRISEA	89	89	89	100	100	97	83	83	75	75	75	78	75	75	75	75	75	75	72	75	75	75	75	75	75	75	75	75	69	69	72	72	75	78	69	72	67	67	64	64	67	64	78	58
MYCOSPHAERELLA-GRAMINICOLA	86	86	89	97	97	100	86	81	72	72	72	75	72	72	72	72	72	72	69	72	72	72	72	72	72	72	72	72	72	72	69	69	78	81	69	69	67	67	64	64	69	64	75	58
CANDIDA-ALBICANS	75	75	81	83	83	86	100	94	69	69	69	72	69	69	69	69	69	69	67	69	69	69	69	69	69	69	69	69	69	69	69	69	75	72	67	69	64	64	61	61	67	61	75	56
PICHIA-STIPITIS	75	75	78	83	83	81	94	100	72	72	72	75	72	72	72	72	72	72	69	72	72	72	72	72	72	72	72	72	67	67	72	72	72	69	67	72	64	64	61	61	64	61	81	56
ARABIDOPSIS-THALIANA	72	72	72	75	75	72	69	72	100	100	97	97	97	97	97	97	97	97	94	94	94	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	69	58
BRASSICA-RAPA-SUBSP.-PEKINENSI	72	72	72	75	75	72	69	72	100	100	97	97	97	97	97	97	97	97	94	94	94	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	69	58
HEVEA-BRASILIENSIS	72	72	72	75	75	72	69	72	97	97	100	97	97	97	97	97	97	97	94	94	94	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	69	58
COPTIS-JAPONICA-VAR.-DISSECTA	75	75	75	78	78	75	72	75	97	97	97	100	97	97	97	97	97	97	94	94	94	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	69	58
SOLENOSTEMON-SCUTELLARIOIDES	72	72	72	75	75	72	69	72	97	97	97	97	100	100	100	100	100	100	97	97	97	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	72	61
AVENA-SATIVA	72	72	72	75	75	72	69	72	97	97	97	97	100	100	100	100	100	100	97	97	97	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	72	61
DAUCUS-CAROTA	72	72	72	75	75	72	69	72	97	97	97	97	100	100	100	100	100	100	97	97	97	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	72	61
SOLANUM-TUBEROSUM	72	72	72	75	75	72	69	72	97	97	97	97	100	100	100	100	100	100	97	97	97	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	72	61
SOLANUM-LYCOPERSICUM	72	72	72	75	75	72	69	72	97	97	97	97	100	100	100	100	100	100	97	97	97	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	72	61
MEDICAGO-TRUNCATULA	72	72	72	75	75	72	69	72	97	97	97	97	100	100	100	100	100	100	97	97	97	94	94	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	72	61
GLYCINE-MAX	69	69	69	72	72	69	67	69	94	94	94	94	97	97	97	97	97	97	100	94	94	92	92	92	92	92	92	89	72	72	75	78	67	69	67	72	64	64	67	67	64	61	69	58
HORDEUM-VULGARE	75	75	75	75	75	72	69	72	94	94	94	94	97	97	97	97	97	97	94	100	100	92	92	94	94	94	97	89	78	78	81	83	72	75	72	78	64	64	67	67	64	67	75	64
ORYZA-SATIVA	75	75	75	75	75	72	69	72	94	94	94	94	97	97	97	97	97	97	94	100	100	92	92	94	94	94	97	89	78	78	81	83	72	75	72	78	64	64	67	67	64	67	75	64
SORGHUM-BICOLOR	72	72	72	75	75	72	69	72	94	94	94	94	94	94	94	94	94	94	92	92	92	100	100	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	69	58
ZEA-MAYS	72	72	72	75	75	72	69	72	94	94	94	94	94	94	94	94	94	94	92	92	92	100	100	94	94	94	94	92	75	75	78	81	69	72	69	75	67	67	69	69	67	64	69	58
ABO95005_OLUCIMARINUS	72	72	72	75	75	72	69	72	94	94	94	94	94	94	94	94	94	94	92	94	94	94	94	100	100	100	97	92	75	75	78	81	69	72	69	75	64	64	67	67	64	64	69	58
OTAURI	72	72	72	75	75	72	69	72	94	94	94	94	94	94	94	94	94	94	92	94	94	94	94	100	100	100	97	92	75	75	78	81	69	72	69	75	64	64	67	67	64	64	69	58
MICROMONAS-PUSILLA-CCMP1545	72	72	72	75	75	72	69	72	94	94	94	94	94	94	94	94	94	94	92	94	94	94	94	100	100	100	97	92	75	75	78	81	69	72	69	75	64	64	67	67	64	64	69	58
TRITICUM-AESTIVUM	75	75	75	75	75	72	69	72	94	94	94	94	94	94	94	94	94	94	92	97	97	94	94	97	97	97	100	92	78	78	81	83	72	75	72	78	64	64	67	67	64	67	72	61
NICOTIANA-BENTHAMIANA	75	75	75	75	75	72	69	72	92	92	92	92	92	92	92	92	92	92	89	89	89	92	92	92	92	92	92	100	78	78	81	83	69	72	72	75	67	67	67	67	67	64	72	61
RHODOCOCCUS-SP.	69	69	78	69	69	72	69	67	75	75	75	75	75	75	75	75	75	75	72	78	78	75	75	75	75	75	78	78	100	97	92	92	83	83	83	78	69	69	69	69	75	69	78	67
RHODOCOCCUS-ERYTHROPOLIS	69	69	78	69	69	72	69	67	75	75	75	75	75	75	75	75	75	75	72	78	78	75	75	75	75	75	78	78	97	100	92	92	83	83	83	78	69	69	69	69	75	69	75	67
STREPTOMYCES-AVERMITILIS	72	72	78	72	72	69	69	72	78	78	78	78	78	78	78	78	78	78	75	81	81	78	78	78	78	78	81	81	92	92	100	94	81	81	83	83	69	69	69	69	72	72	78	67
JANIBACTER-SP.-HTCC2649	72	72	78	72	72	69	69	72	81	81	81	81	81	81	81	81	81	81	78	83	83	81	81	81	81	81	83	83	92	92	94	100	81	83	83	83	69	69	69	69	72	69	78	67
KORDIA-ALGICIDA	69	69	78	75	75	78	75	72	69	69	69	69	69	69	69	69	69	69	67	72	72	69	69	69	69	69	72	69	83	83	81	81	100	86	83	83	75	75	72	72	78	72	75	64
LEEUWENHOEKIELLA-BLANDENSIS-ME	72	72	81	78	78	81	72	69	72	72	72	72	72	72	72	72	72	72	69	75	75	72	72	72	72	72	75	72	83	83	81	83	86	100	83	83	72	72	69	69	78	72	72	64
PICROPHILUS-TORRIDUS	69	69	78	69	69	69	67	67	69	69	69	69	69	69	69	69	69	69	67	72	72	69	69	69	69	69	72	72	83	83	83	83	83	83	100	86	69	69	69	69	72	69	75	69
GEMMATIMONAS-AURANTIACA	69	69	72	72	72	69	69	72	75	75	75	75	75	75	75	75	75	75	72	78	78	75	75	75	75	75	78	75	78	78	83	83	83	83	86	100	72	72	69	69	75	72	72	69
VIBRIO-SP.-MED222	58	58	69	67	67	67	64	64	67	67	67	67	67	67	67	67	67	67	64	64	64	67	67	64	64	64	64	67	69	69	69	69	75	72	69	72	100	100	94	94	92	81	64	61
MARINOMONAS-SP.-MED121	58	58	69	67	67	67	64	64	67	67	67	67	67	67	67	67	67	67	64	64	64	67	67	64	64	64	64	67	69	69	69	69	75	72	69	72	100	100	94	94	92	81	64	61
SULFITOBACTER-SP.-NAS-14.1	58	58	69	64	64	64	61	61	69	69	69	69	69	69	69	69	69	69	67	67	67	69	69	67	67	67	67	67	69	69	69	69	72	69	69	69	94	94	100	100	86	75	64	61
OCEANICOLA-BATSENSIS-HTCC2597	58	58	69	64	64	64	61	61	69	69	69	69	69	69	69	69	69	69	67	67	67	69	69	67	67	67	67	67	69	69	69	69	72	69	69	69	94	94	100	100	86	75	64	61
PSEDUMONOASE-FLUORESCENCE	58	58	67	67	67	69	67	64	67	67	67	67	67	67	67	67	67	67	64	64	64	67	67	64	64	64	64	67	75	75	72	72	78	78	72	75	92	92	86	86	100	81	64	61
BDELLOVIBRIO-BACTERIOVORUS	61	61	67	64	64	64	61	61	64	64	64	64	64	64	64	64	64	64	61	67	67	64	64	64	64	64	67	64	69	69	72	69	72	72	69	72	81	81	75	75	81	100	64	61
BLEPHARISMA-JAPONICUS	81	81	83	78	78	75	75	81	69	69	69	69	72	72	72	72	72	72	69	75	75	69	69	69	69	69	72	72	78	75	78	78	75	72	75	72	64	64	64	64	64	64	100	72
SYNECHOCOCCUS-SP.	64	64	67	58	58	58	56	56	58	58	58	58	61	61	61	61	61	61	58	64	64	58	58	58	58	58	61	61	67	67	67	67	64	64	69	69	61	61	61	61	61	61	72	100

Table 5a: Amino acid positions which are strictly conserved shown for the crystal structures

Arabidopsis thaliana		*Pseudomonas fluorescens*		*Streptomyces avermitilis*		*Homo sapiens*		*Rattus norvegicus*	
Position	Amino Acid	Position	Amino Acid	Position	Amino Acid	Position	Amino Acid	Position	Amino Acid
226	H	162	H	187	H	183	H	183	H
267	S	202	S	230	S	226	S	226	S
282	N	217	N	245	N	241	N	241	N
308	H	241	H	270	H	266	H	266	H
342	Y	271	Y	299	Y	295	Y	295	Y
394	E	323	E	349	E	349	E	349	E
420	G	334	G	360	G	360	G	360	G
423	N	337	N	363	N	363	N	363	N

Table 5b: Amino acid position with the amino acids at this positions in the known crystal structures and the amino acids a these position within all HPPD sequences

Arabidopsis thaliana		*Pseudomonas fluorescens*		*Streptomyces avermitilis*		*Homo sapiens*		*Rattus norvegicus*		Natural Variabaility
Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Amino Acid
228	V	164	T	189	V	185	V	185	V	VTCAG
248	H	186	R	211	T	207	H	207	H	HRQTKEYLAGSN
250	F	188	A	213	M	209	F	209	F	FYILVAQEDGTSMRK
251	A	189	R	214	K	210	W	210	W	AWILSRKHDEPGNY
252	E	190	Y	215	E	211	S	211	S	ESTYFHQNGLMVILIR
253	F	191	F	216	F	212	V	212	V	FVIALWMQHY
265	L	200	L	228	L	224	L	224	L	LMVIA
268	A	203	K	231	K	227	I	227	I	AVLMIKRQY
269	V	204	A	232	V	228	V	228	V	VAT
270	L	205	M	233	V	229	V	229	V	LVMIA
271	A	206	S	234	A	230	A	230	A	ASTVRKELIMHG
280	P	215	P	243	P	239	P	239	P	PAVTNI
293	Q	226	Q	255	Q	251	Q	251	Q	QLAVRSGVFM
294	I	227	I	256	I	252	I	252	I	IMVTASP
307	Q	240	Q	269	Q	265	Q	265	Q	QHN
335	M	264	M	293	L	289	L	289	L	MLIN
368	L	295	L	323	L	323	L	323	L	LM
379	Q	310	Q	334	Q	334	Q	334	Q	QH
381	F	312	F	336	F	336	F	336	F	FY
392	F	321	F	347	F	347	F	347	F	FS
419	F	333	F	359	F	359	F	359	F	FY
421	K	335	E	361	K	361	A	361	A	KQAILVNDEGS
422	G	336	G	362	G	362	G	362	G	GAPVTM
424	F	338	F	364	F	364	F	364	F	FAVIL
425	S	339	K	365	K	365	N	365	N	SNKGRAPSIKQR
426	E	340	A	366	A	366	S	366	S	EQSAIVFT
427	L	341	L	367	L	367	L	367	L	LR
431	I	345	I	371	I	371	F	371	F	IFVMLQR

Table 5c: Amino acid position with the amino acids at this positions in the known crystal structures and most common amino acids a these position within all HPPD sequences

Arabidopsis thaliana		Pseudomonas fluorescens		Streptomyces avermitilis		Homo sapiens		Rattus norvegicus		Most common
Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Amino Acid
228	V	164	T	189	V	185	V	185	V	VTCA
248	H	186	R	211	T	207	H	207	H	HRQTKEYA
250	F	188	A	213	M	209	F	209	F	FYILVAEDTM
251	A	189	R	214	K	210	W	210	W	AWILRKHDEPY
252	E	190	Y	215	E	211	S	211	S	ESTRY
253	F	191	F	216	F	212	V	212	V	FVIALWY
265	L	200	L	228	L	224	L	224	L	LMVA
268	A	203	K	231	K	227	I	227	I	AVLMIKRQY
269	V	204	A	232	V	228	V	228	V	VA
270	L	205	M	233	V	229	V	229	V	LVMI
271	A	206	S	234	A	230	A	230	A	ASTVREGK
280	P	215	P	243	P	239	P	239	P	PAVT
293	Q	226	Q	255	Q	251	Q	251	Q	QLA
294	I	227	I	256	I	252	I	252	I	IMVA
307	Q	240	Q	269	Q	265	Q	265	Q	QHN
335	M	264	M	293	L	289	L	289	L	MLI
368	L	295	L	323	L	323	L	323	L	LM
379	Q	310	Q	334	Q	334	Q	334	Q	QH
381	F	312	F	336	F	336	F	336	F	FY
392	F	321	F	347	F	347	F	347	F	F
419	F	333	F	359	F	359	F	359	F	FY
421	K	335	E	361	K	361	A	361	A	KQAIVLDE
422	G	336	G	362	G	362	G	362	G	GA
424	F	338	F	364	F	364	F	364	F	FAVL
425	S	339	K	365	K	365	N	365	N	SNKRAIQ
426	E	340	A	366	A	366	S	366	S	ESAIVF
427	L	341	L	367	L	367	L	367	L	LR
431	I	345	I	371	I	371	F	371	F	IFVMQRL

[0046] Not all amino acids occurring at the variable positions have the same likelihood to be present in an active protein. In some cases most sequences have the same amino acids at a particular position while other amino acids are present at that position in only few HPPD sequences. An example is position 392. Most sequences have at a corresponding position a phenylalanine while few i.e. the *burkholderia* sequences have a serine. Whereas in some rare cases, the rare amino acids may be the result of a sequencing error, in most other cases the resulting protein is active. Table 5c shows a list with the most common amino acids at the variable positions.

[0047] The influence of the amino acids at the variable positions is different. Some of these positions are crucial for catalysis and/or the interaction of HPPD with an inhibitor while others may have less impact. For instances changes at positions 269 and 280 which are in direct contact with the inhibitor and the substrate will very likely have a great impact upon catalysis and inhibitor binding. Also modifications at positions involved in the helix movement induced by inhibitor or substrate binding such as positions 252, 421 and 422 are likely to have high impact on inhibitor binding. In contrast modifications at positions such as 293 are less likely to influence inhibitor binding because this position is quite distant from the active site. Table 6a shows the position with very high impact and table 6b with impact on activity and inhibitor binding.

[0048] From these observations, the present inventors drew the conclusion that amino acids are preferred in the binding sites wich naturally occur at the corresponding positions. This means, that those modifications which exchange a naturally occurring amino acid into another are likely providing a catalytically active HPPD protein which may exert a modified or even increased tolerance to HPPD herbicide inhibitors. Even rmore promising are those mutant proteins which have the amino acid most often found in nature at the variable position chosen from Table 5c.

Table 6a: Amino acid positions with high priority shown for the x-ray structures

Arabidopsis thaliana		*Pseudomonas fluorescens*		*Streptomyces avermitilis*		*Homo sapiens*		*Rattus norvegicus*	
Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid
228	V	164	T	189	V	185	V	185	V
250	F	188	A	213	M	209	F	209	F
251	A	189	R	214	K	210	W	210	W
252	E	190	Y	215	E	211	S	211	S
253	F	191	F	216	F	212	V	212	V
265	L	200	L	228	L	224	L	224	L
268	A	203	K	231	K	227	I	227	I
269	V	204	A	232	V	228	V	228	V
270	L	205	M	233	V	229	V	229	V
271	A	206	S	234	A	230	A	230	A
280	P	215	P	243	P	239	P	239	P
307	Q	240	Q	269	Q	265	Q	265	Q
335	M	264	M	293	L	289	L	289	L
368	L	295	L	323	L	323	L	323	L
379	Q	310	Q	334	Q	334	Q	334	Q
392	F	321	F	347	F	347	F	347	F
421	K	335	E	361	K	361	A	361	A
422	G	336	G	362	G	362	G	362	G
426	E	340	A	366	A	366	S	366	S
427	L	341	L	367	L	367	L	367	L

Table 6b: Amino acid positions with very high priority shown for the x-ray structures

Arabidopsis thaliana		*Pseudomonas fluorescens*		*Streptomyces avermitilis*		*Homo sapiens*		*Rattus norvegicus*	
Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid	Pos.	Amino Acid
252	E	190	Y	215	E	211	S	211	S
269	V	204	A	232	V	228	V	228	V
280	P	215	P	243	P	239	P	239	P
335	M	264	M	293	L	289	L	289	L
368	L	295	L	323	L	323	L	323	L
421	K	335	E	361	K	361	A	361	A
422	G	336	G	362	G	362	G	362	G

[0049] In another embodiment, in the isolated nucleic acid of the invention as defined above, said at least on amino acid is selected from

a) Ala, Asp, Glu, Phe, Thr, Val or Tyr at a position in an HPPD protein, said position corresponding to position 250 of the amino acid sequence of SEQ ID No. 2;
b) Ala, Asp, Glu, Ile, Lys, Leu, Pro or Arg at a position in an HPPD protein, said position corresponding to position 251 of the amino acid sequence of SEQ ID No. 2;
c) Glu, Thr, Arg, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 252 of the amino

acid sequence of SEQ ID No. 2;
d) Ala, Phe, Val or Trp at a position in an HPPD protein, said position corresponding to position 253 of the amino acid sequence of SEQ ID No. 2;
e) Leu or Val at a position in an HPPD protein, said position corresponding to position 265 of the amino acid sequence of SEQ ID No. 2;
f) Leu, Gln, Arg, Val or Tyr at a position in an HPPD protein, said position corresponding to position 268 of the amino acid sequence of SEQ ID NO: 2;
g) Ala or Val at a position in an HPPD protein, said position corresponding to position 269 of the amino acid sequence of SEQ ID No. 2;
h) Ala, Pro, Thr or Val at a position in an HPPD protein, said position corresponding to position 280 of the amino acid sequence of SEQ ID No. 2;
i) Gln at a position in an HPPD protein, said position corresponding to position 307 of the amino acid sequence of SEQ ID No. 2;
j) Ile or Met at a position in an HPPD protein, said position corresponding to position 335 of the amino acid sequence of SEQ ID No. 2;
k) Leu at a position in an HPPD protein, said position corresponding to position 368 of the amino acid sequence of SEQ ID No. 2;
l) Phe at a position in an HPPD protein, said position corresponding to position 392 of the amino acid sequence of SEQ ID No. 2;
m) Asp, Lys, or Asn at a position in an HPPD protein, said position corresponding to position 421 of the amino acid sequence of SEQ ID No. 2;
n) Ala or Gly at a position in an HPPD protein, said position corresponding to position 422 of the amino acid sequence of SEQ ID No. 2;
o) Ile, Arg or Ser at a position in an HPPD protein, said position corresponding to position 425 of the amino acid sequence of SEQ ID No. 2
p) Glu, Phe or Val at a position in an HPPD protein, said position corresponding to position 426 of the amino acid sequence of SEQ ID No. 2;
q) Ile, Met, Gln or Val or Phe at a position in an HPPD protein, said position corresponding to position 431 of the amino acid sequence of SEQ ID No. 2;
r) Ala, Cys, Thr or Val at a position in an HPPD protein, said position corresponding to position 228 of the amino acid sequence of SEQ ID No. 2;
s) Ala, Glu, His, Lys, Gln, Arg, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 248 of the amino acid sequence of SEQ ID No. 2;
t) Ile, Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 270 of the amino acid sequence of SEQ ID No. 2;
u) Ala, Glu, Lys, Arg, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 271 of the amino acid sequence of SEQ ID No. 2;
v) His or Gln at a position in an HPPD protein, said position corresponding to position 379 of the amino acid sequence of SEQ ID No. 2;
w) Leu or Arg at a position in an HPPD protein, said position corresponding to position 427 of the amino acid sequence of SEQ ID No. 2.

[0050] In an alternative embodiment of the nucleic acid of the invention, said at least one amino acid is selected from

a) Glu, Thr, Arg, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 2;
b) Ala or Val at a position in an HPPD protein, said position corresponding to position 269 of the amino acid sequence of SEQ ID No. 2;
c) Ala, Pro, Thr or Val at a position in an HPPD protein, said position corresponding to position 280 of the amino acid sequence of SEQ ID No. 2;
d) Ile or Met at a position in an HPPD protein, said position corresponding to position 335 of the amino acid sequence of SEQ ID No. 2;
e) Leu at a position in an HPPD protein, said position corresponding to position 368 of the amino acid sequence of SEQ ID No. 2;
f) Asp,, Asn or Lys at a position in an HPPD protein, said position corresponding to position 421 of the amino acid sequence of SEQ ID No. 2;
g) Ala or Gly at a position in an HPPD protein, said position corresponding to position 422 of the amino acid sequence of SEQ ID No. 2;

h) Ala, Cys, Thr or Val at a position in an HPPD protein, said position corresponding to position 228 of the amino acid sequence of SEQ ID No. 2;

i) Ala, Glu, His, Lys, Gln, Arg, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 248 of the amino acid sequence of SEQ ID No. 2;

j) Ile, Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 270 of the amino acid sequence of SEQ ID No. 2;

k) Ala, Glu, Lys, Arg, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 271 of the amino acid sequence of SEQ ID No. 2;

l) His or Gln at a position in an HPPD protein, said position corresponding to position 379 of the amino acid sequence of SEQ ID No. 2;

m) Leu or Arg at a position in an HPPD protein, said position corresponding to position 427 of the amino acid sequence of SEQ ID No. 2.

[0051] Various sequences of HPPD proteins or predicted HPPD proteins are known in the art. These include the HPPD sequences of Streptomyces avermitilis (Genebank SAV11864), Daucus carota (Genebank DCU 87257), Arabidopsis thaliana (Genebank AF047834), Mycosphaerella graminicola (Genebank AF038152), oryza sativa / rice [BAD26248], Zea mays / corn [ACN36372], avena sativa [ABZ23427], Pseudomonas fluorescens [ABF50055], Synechococcus sp. [YP_473959], Blepharisma japonicum [BAF91881], Rhodococcus RHA1 sp. ro0240 [YP_702005], Rhodococcus RHA1 sp. ro0341 [YP_703002], Picrophilus torridus [YP_024147], Kordia algicida [ZP_02161490], Sorghum bicolor [XP_002453359], Triticum aestivum / wheat [AAZ67144], or Hordeum vulgare / barley [O48604].

[0052] The sequence of the HPPD protein taken as a starting point may be any amino acid sequence encoding a catalytically active HPPD protein. In one embodiment of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 4 [Oryza sativa], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile, Leu or Met at position 247 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 250 of SEQ ID No. 2);

b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg, Ser, Gly, His or Tyr at position 248 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 251 of SEQ ID No. 2);

c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Tyr or Thr at position 249 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 252 of SEQ ID No. 2) ;

d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 250 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 253 of SEQ ID No. 2);

e) Val or Met at position 262 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 265 of SEQ ID No. 2);

f) Leu, Gln, Arg, Tyr, Ala, Ile, Lys or Met at position 265 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 268 of SEQ ID No. 2);

g) Ala or Thr at position 266 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 269 of SEQ ID No. 2);

h) Ala, Ile, Asn, Thr or Val at position 277 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 280 of SEQ ID No. 2);

i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 290 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 293 of SEQ ID No. 2);

j) Met, Ala, Pro, Ser, Thr or Val at position 291 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 294 of SEQ ID No. 2);

k) Ile, Met or Asn at position 332 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 335 of SEQ ID No. 2);

l) Met at position 365 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 368 of SEQ ID No. 2);

m) Tyr at position 378 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 381 of SEQ ID No. 2);

n) Ser at position 389 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 392 of SEQ ID No. 2);

o) Tyr at position 416 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 419 of SEQ ID No. 2);

p) Asp, Phe, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 418 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 421 of SEQ ID No. 2);

q) Ala, Met, Pro or Thr at position 419 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 422 of SEQ ID No. 2);

r) Ala, Ile or Val at position 421 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 424 of SEQ ID No. 2);

s) Ile, Pro, Arg, Ala, Gly, Lys, Asn or Gln at position 422 of the amino acid sequence of SEQ ID No. 4 (corresponding

to position 425 of SEQ ID No. 2);
t) Phe, Thr, Val, Ala, Gln or Ser at position 423 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 426 of SEQ ID No. 2);
u) Met, Gln, Val, Phe or Leu at position 428 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 431 of SEQ ID No. 2);
v) Phe at position 431 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 434 of SEQ ID No. 2);
w) Ala, Cys, Gly or Thr at position 225 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 245 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Met or Val at position 267 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 270 of SEQ ID No. 2);
z) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 268 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 271 of SEQ ID No. 2);
aa)His at position 376 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 379 of SEQ ID No. 2);
bb)Arg at a position in an HPPD protein, said position corresponding to position 424 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 427 of SEQ ID No. 2).

[0053] In another embodiment of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 6 [Zea mays], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile, Leu or Met at position 224 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 250 of SEQ ID No. 2);
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg, Ser, Gly, His or Tyr at position 225 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 251 of SEQ ID No. 2);
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Tyr or Thr at position 226 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 252 of SEQ ID No. 2);
d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 227 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 253 of SEQ ID No. 2);
e) Val or Met at position 239 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val, Tyr, Ala, Ile or Lys at position 242 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 243 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 269 of SEQ ID No. 2);
h) Ala, Ile, Asn, Thr or Val at position 254 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 280 of SEQ ID No. 2);
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 267 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 268 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 281 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 307 of SEQ ID No. 2);
l) Ile, Asn or Leu at position 309 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 335 of SEQ ID No. 2);
m) Met at position 342 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 368 of SEQ ID No. 2);
n) Tyr at position 355 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 366 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 392 of SEQ ID No. 2);
p) Tyr at position 393 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Phe, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 395 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 421 of SEQ ID No. 2);
r) Ala, Met, Pro or Thr at position 396 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 398 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Arg, Ala, Gly, Lys, Asn or Gln at position 399 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 425 of SEQ ID No. 2);
u) Glu, Phe, Thr, Val, Ala or Ser at position 400 of the amino acid sequence of SEQ ID No. 6 (corresponding to

position 426 of SEQ ID No. 2);

v) Met, Gln, Val, Phe or Leu at position 405 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 431 of SEQ ID No. 2);

w) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 202 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 228 of SEQ ID No. 2);

x) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 222 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 248 of SEQ ID No. 2);

y) Ala, Ile, Met or Val at position 244 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 270 of SEQ ID No. 2);

z) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 245 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 271 of SEQ ID No. 2);

aa) Gln at position 353 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 379 of SEQ ID No. 2);

ab) Arg at position 401 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 427 of SEQ ID No. 2).

[0054] In another embodiment of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 8 [Avena sativa], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile, Leu or Met at position 241 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 250 of SEQ ID No. 2), preferably Ala ;

b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg, Ser, Gly, His or Tyr at position 242 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;

c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Tyr or Thr at position 243 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 252 of SEQ ID No. 2), preferably Tyr;

d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 244 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 253 of SEQ ID No. 2), preferably Val;

e) Val or Met at position 256 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 265 of SEQ ID No. 2);

f) Leu, Gln, Arg, Tyr, Ala, Ile, Lys or Met at position 259 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 268 of SEQ ID No. 2);

g) Ala or Thr at position 260 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;

h) Ala, Ile, Asn, Thr or Val at position 271 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 280 of SEQ ID No. 2);

i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 284 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 293 of SEQ ID No. 2);

j) Met, Ala, Pro, Ser, Thr or Val at position 285 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 294 of SEQ ID No. 2);

k) His or Asn at position 265 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 307 of SEQ ID No. 2);

l) Ile or Asn or Leu at position 326 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 335 of SEQ ID No. 2);

m) Met at position 359 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 368 of SEQ ID No. 2);

n) Tyr at position 372 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 381 of SEQ ID No. 2);

o) Ser at position 383 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 392 of SEQ ID No. 2);

p) Tyr at position 410 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 419 of SEQ ID No. 2);

q) Asp, Phe, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 412 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;

r) Ala, Met, Pro or Thr at position 413 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 422 of SEQ ID No. 2);

s) Ala, Ile or Val at position 415 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 424 of SEQ ID No. 2);

t) Ile, Pro, Arg, Ala, Gly, Lys, Asn or Gln at position 416 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 425 of SEQ ID No. 2);

u) Phe, Thr, Val, Ala, Gln or Ser at position 417 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 426 of SEQ ID No. 2);

v) Met, Gln, Val, Phe or Leu at position 422 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 431 of SEQ ID No. 2);

w) Ala, Cys, Gly or Thr at position 219 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 239 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Met or Val at position 261 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 270 of SEQ ID No. 2);
z) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 262 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 271 of SEQ ID No. 2);
aa) His at position 370 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 379 of SEQ ID No. 2);
bb) Arg at position 418 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 427 of SEQ ID No. 2).

[0055] In another embodiment, of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 10 [Pseudomonas fluorescens], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Phe, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile, Leu or Met at position 188 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 250 of SEQ ID No. 2), preferably Ala;
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Ser, Gly, His or Tyr at position 189 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 251 of SEQ ID No. 2), preferably Ala or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Glu or Thr at position 190 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 252 of SEQ ID No. 2), preferably Ser or Tyr;
d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 191 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 253 of SEQ ID No. 2), preferably Phe or Val;
e) Val or Met at position 200 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val Tyr, Ala, Ile or Met at position 203 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 268 of SEQ ID No. 2);
g) Thr or Val at position 204 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 269 of SEQ ID No. 2), preferably Val;
h) Ala, Ile, Asn, Thr or Val at position 215 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 280 of SEQ ID No. 2);
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 226 of the amino acid sequence of SEQ ID NO:SEQ ID No. 10 (corresponding to position 293 of SEQ ID No. 2);
j) Met, Thr, Ala, Pro, Ser or Val at position 227 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 240 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 307 of SEQ ID No. 2);
l) Ile, Asn or Leu at position 264 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 335 of SEQ ID No. 2);
m) Met at position 295 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 368 of SEQ ID No. 2);
n) Tyr at position 312 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 321 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 392 of SEQ ID No. 2);
p) Tyr at position 333 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Lys, Asn, Ala, Cys, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 335 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
r) Ala, Met, Pro or Thr at position 336 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 338 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Ala, Asn, Gly or Gln at position 339 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 425 of SEQ ID No. 2);
u) Phe, Thr or Val at position 340 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 426 of SEQ ID No. 2);
v) Met, Phe, Leu, Gln or Val at position 345 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 431 of SEQ ID No. 2);
w) Ala, Cys, Gly or Val at position 164 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Ser, Thr or Tyr at position 186 of the amino acid sequence of SEQ ID No.

10 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Leu or Val at position 205 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 270 of SEQ ID No. 2);
z) Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Thr or Val at position 206 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 271 of SEQ ID No. 2);
aa) His at position 310 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 379 of SEQ ID No. 2);
bb) Arg at position 341 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 427 of SEQ ID No. 2).

[0056] In another embodiment of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 14 [Synechococcus sp.], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile or Met at position 169 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 250 of SEQ ID No. 2), preferably Ala or Phe;
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser, Gly or His at position 170 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 251 of SEQ ID No. 2), preferably Ala, Arg or Lys;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Ser, Val, Tyr or Thr at position 171 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 252 of SEQ ID No. 2), preferably Glu, Ser or Tyr;
d) Ala, Phe, His, Gln, Val or Ile, Leu or Met at position 172 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 253 of SEQ ID No. 2), preferably Phe or Val;
e) Val or Met at position 181 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Tyr, Ala, Ile, Lys or Met at position 184 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 185 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 269 of SEQ ID No. 2), preferably Ala ;
h) Ile, Asn, Pro, Thr or Val at position 196 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 280 of SEQ ID No. 2), preferably Pro;
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 206 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 293 of SEQ ID No. 2);
j) Met , Ala, Pro, Ser, Thr or Val at position 207 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 220 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 307 of SEQ ID No. 2);
l) Ile, Met or Asn at position 244 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
m) Met at position 286 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 368 of SEQ ID No. 2);
n) Phe or Tyr at position 301 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 312 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 392 of SEQ ID No. 2);
p) Tyr at position 325 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Phe, Lys, Asn, Ala, Cys, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 327 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
r) Gly, Met, Pro or Thr at position 328 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 330 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Arg, Ser, Ala, Gly, Lys or Asn at position 331 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 425 of SEQ ID No. 2);
u) Glu, Phe, Thr, Val, Gln or Ser at position 332 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
v) Ile, Met, Gln, Val or Phe at position 337 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 431 of SEQ ID No. 2);
w) Ala, Cys, Gly or Thr at position 145 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Ser, Thr or Tyr at position 167 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Leu or Met at position 186 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 270

of SEQ ID No. 2);
z) Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 187 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 271 of SEQ ID No. 2);
aa) His at a position at position 299 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 379 of SEQ ID No. 2);
bb) Arg at a position at position 333 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 427 of SEQ ID No. 2).

[0057] In another embodiment of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 16 [Blepharisma japonicum], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val, Ile, Leu or Met at position 209 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 250 of SEQ ID No. 2), preferably Ala or Phe;
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg, Ser, Gly, His or Tyr at position 210 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 251 of SEQ ID No. 2), preferably Ala, Arg, Lys;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Val, Tyr or Thr at position 211 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 252 of SEQ ID No. 2), preferably Glu or Tyr;
d) Phe, His, Gln, Val, Trp, Ile, Leu or Met at position 212 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 253 of SEQ ID No. 2), preferably Phe or Val;
e) Val or Met at position 224 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Tyr, Ala, Ile, Lys or Met at position 227 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 2268 of SEQ ID No. 2);
g) Ala or Thr at position 228 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 239 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 280 of SEQ ID No. 2);
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 251 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 293 of SEQ ID No. 2);
j) Met, Ala, Pro, Ser, Thr or Val at position 252 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 265 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 307 of SEQ ID No. 2);
l) Ile, Met or Asn at position 289 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
m) Met at position 323 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 368 of SEQ ID No. 2);
n) Tyr at position 336 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 347 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 292 of SEQ ID No. 2);
p) Tyr at position 359 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Phe, Lys, Asn, Ala, Cys, Glu, Gly, His, Leu, Met, Gln, Ser, Thr or Val at position 361 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
r) Ala, Met, Pro or Thr at position 362 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 364 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Arg, Ser, Ala, Gly, Asn or Gln at position 365 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 425 of SEQ ID No. 2);
u) Glu, Phe, Thr, Val, Gln or Ser at position 366 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
v) Ile, Met, Gln, Val or Phe at position 371 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 431 of SEQ ID No. 2);
w) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 185 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 207 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Leu or Met at a position in an HPPD protein, said position corresponding to position 229 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 270 of SEQ ID No. 2);

z) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 230 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 271 of SEQ ID No. 2);
aa) His at a position in an HPPD protein, said position corresponding to position 334 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 379 of SEQ ID No. 2);
bb) Arg at a position in an HPPD protein, said position corresponding to position 367 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 427 of SEQ ID No. 2).

[0058] In another embodiment, of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 18 [Rhodococcus RHA1 sp. ro0240], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile or Leu at position 231 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 250 of SEQ ID No. 2), preferably Phe or Ala;
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg, Ser, Gly, His or Tyr at position 232 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Tyr or Thr at position 233 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 252 of SEQ ID No. 2), preferably Ser or Tyr;
d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 234 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val or Met at position 246 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val, Tyr, Ala, Ile or Met at position 249 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 250 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 261 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 280 of SEQ ID No. 2);
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 273 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 293 of SEQ ID No. 2);
j) Met, Ala, Pro, Ser, Thr or Val at position 274 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 287 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 307 of SEQ ID No. 2);
l) Ile, Met or Asn at position 311 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
m) Met at position 343 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 368 of SEQ ID No. 2);
n) Tyr at position 356 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 367 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 392 of SEQ ID No. 2);
p) Tyr at position 379 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Lys, Asn, Ala, Cys, Glu, Gly, His, Leu, Met, Gln, Ser, Thr or Val at position 381 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
r) Ala, Met, Pro or Thr at position 382 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 384 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Arg, Ser, Ala, Gly, Asn or Gln at position 385 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 425 of SEQ ID No. 2);
u) Glu, Phe, Thr, Val, Gln or Ser at position 386 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
v) Met, Gln, Phe, Val, Phe or Leu at position 391 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 431 of SEQ ID No. 2);
w) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 207 of the amino acid sequence of SEQ ID No. 1 (corresponding to position 228 of SEQ ID No. 2)8;
x) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 229 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Leu or Met at a position in an HPPD protein, said position corresponding to position 251 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 270 of SEQ ID No. 2);
z) Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Thr or Val at a position in an HPPD protein, said position corresponding to

position 252 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 271 of SEQ ID No. 2);
aa) His at a position in an HPPD protein, said position corresponding to position 354 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 379 of SEQ ID No. 2);
bb) Arg at a position in an HPPD protein, said position corresponding to position 387 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 427 of SEQ ID No. 2).

[0059] In another embodiment, of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 30 [Rhodococcus RHA1 sp. 0341], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile or Leu at position 232 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 250 of SEQ ID No. 2), preferably Phe or Ala;
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg, Ser, Gly, His or Tyr at position 233 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Tyr or Thr at position 234 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 252 of SEQ ID No. 2), preferably Ser or Tyr;
d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 235 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val or Met at position 247 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val, Tyr, Ala, Ile or Met at position 250 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 251 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 262 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 280 of SEQ ID No. 2);
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 274 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 293 of SEQ ID No. 2);
j) Met, Ala, Pro, Ser, Thr or Val at position 275 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 288 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 307 of SEQ ID No. 2);
l) Ile, Met or Asn at position 312 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
m) Met at position 344 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 368 of SEQ ID No. 2);
n) Tyr at position 357 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 368 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 392 of SEQ ID No. 2);
p) Tyr at position 380 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Phe, Lys, Asn, Ala, Cys, Glu, Gly, His, Leu, Met, Gln, Ser, Thr or Val at position 382 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
r) Ala, Met, Pro or Thr at position 383 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 385 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Arg, Ser, Ala, Gly, Asn or Gln at position 386 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 425 of SEQ ID No. 2);
u) Glu, Phe, Thr, Val, Gln or Ser at position 387 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
v) Met, Gln, Phe, Val, Phe or Leu at position 392 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 431 of SEQ ID No. 2);
w) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 208 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 230 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Leu or Met at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 270 of SEQ ID No. 2);
z) Glu, His, Ile, Lys, Leu, Met, Arg, Thr or Val at a position in an HPPD protein, said position corresponding to position 253 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 271 of SEQ ID No. 2);

aa)His at a position in an HPPD protein, said position corresponding to position 355 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 379 of SEQ ID No. 2);
bb)Arg at a position in an HPPD protein, said position corresponding to position 388 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 427 of SEQ ID No. 2).

[0060] In another embodiment, of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 20 [Picrophilus torridus], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile or Met at position 201 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 250 of SEQ ID No. 2), preferably Phe or Ala;
b) Ala, Asp, Glu, Lys, Leu, Asn, Pro, Arg or Ser, Gly, His or Trp at position 202 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 251 of SEQ ID No. 2), preferably Ala, Arg or Lys;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at position 203 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 252 of SEQ ID No. 2), preferably Glu, Ser or Tyr;
d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 204 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val or Met at position 216 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val, Tyr, Ala, Ile or Met at position 219 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 220 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 230 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 280 of SEQ ID No. 2);
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 242 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 293 of SEQ ID No. 2);
j) Met, Ala, Pro, Ser, Thr or Val at position 243 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 256 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 307 of SEQ ID No. 2);
1) Ile, Met or Asn at position 280 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
m) Met at position 310 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 368 of SEQ ID No. 2);
n) Phe or Tyr at position 323 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 334 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 392 of SEQ ID No. 2);
p) Tyr at position 346 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Phe, Lys, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 348 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
r) Ala, Met, Pro or Thr at position 349 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 351 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Arg, Ser, Ala, Gly, Lys or Gln at position 352 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 425 of SEQ ID No. 2);
u) Glu, Phe, Thr, Val, Ala or Gln at position 353 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
v) Met, Gln, Phe, Val, Phe or Leu at position 358 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 431 of SEQ ID No. 2);
w) Ala, Cys, Gly or Thr at position 177 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 199 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Leu or Met at a position at position 221 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 270 of SEQ ID No. 2);
z) Ala, Glu, His, Ile, Leu, Met, Arg, Ser, Thr or Val at position 222 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 271 of SEQ ID No. 2);

aa) His at position 321 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 379 of SEQ ID No. 2);
bb) Arg at position 354 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 427 of SEQ ID No. 2).

[0061] In another embodiment, of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 22 [Kordia algicida], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Leu or Met at position 219 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 250 of SEQ ID No. 2), preferably Phe or Ala;
b) Ala, Asp, Glu, Lys, Leu, Asn, Pro, Arg or Ser, Gly, His or Trp at position 220 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 251 of SEQ ID No. 2), preferably Ala, Arg or Lys;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Val, Tyr or Thr at position 221 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 252 of SEQ ID No. 2), preferably Glu or Tyr;
d) Ala, His, Gln, Val Trp, Ile, Leu or Met at position 222 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val or Met at position 234 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val, Tyr, Ala, Ile or Met at position 237 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 238 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 249 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 280 of SEQ ID No. 2);
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 261 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 293 of SEQ ID No. 2);
j) Met, Ala, Pro, Ser, Thr or Val at position 262 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 275 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 307 of SEQ ID No. 2);
l) Ile, Met or Asn at position 299 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
m) Met at position 329 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 368 of SEQ ID No. 2);
n) Tyr at position 342 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 353 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 392 of SEQ ID No. 2);
p) Tyr at position 365 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Phe, Lys, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser or Thr at position 367 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
r) Ala, Met, Pro or Thr at position 368 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 370 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Arg, Ser, Ala, Gly, Asn or Gln at position 371 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 425 of SEQ ID No. 2);
u) Glu, Phe, Thr, Val, Gln or Ser at position 372 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
v) Met, Gln, Phe, Val, Phe or Leu at position 377 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 431 of SEQ ID No. 2);
w) Ala, Cys, Gly or Thr at position 195 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 228 of SEQ ID No. 2);
x) Glu, Gly, His, Lys, Leu, Asn, Gin, Arg, Ser, Thr or Tyr at position 217 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Leu or Val at position 239 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 270 of SEQ ID No. 2);
z) Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Thr or Val at position 240 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 271 of SEQ ID No. 2);
aa) His at a position at position 340 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 379

of SEQ ID No. 2);

bb) Arg at a position at position 373 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 427 of SEQ ID No. 2).

[0062] In another embodiment, of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 24 [Sorghum bicolor], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys,Gln, Arg, Ser, Thr, Val Tyr, Ile, Leu or Met at position 241 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 250 of SEQ ID No. 2), preferably Ala;

b) Asp, Glu, Lys, Leu, Asn, Pro, Arg, Ser, Gly, His or Trp at position 242 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;

c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Val, Tyr or Thr at position 243 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 252 of SEQ ID No. 2), preferably Tyr;

d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 244 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 253 of SEQ ID No. 2), preferably Val;

e) Val or Met at position 256 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 265 of SEQ ID No. 2);

f) Leu, Gln, Arg, Val, Tyr, Ala, Ile or Lys at position 259 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 268 of SEQ ID No. 2);

g) Ala or Thr at position 260 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;

h) Ala, Ile, Asn, Thr or Val at position 271 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 280 of SEQ ID No. 2);

i) Leu or Val, Ala, Phe, Gly, Met, Arg or Ser at position 284 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 293 of SEQ ID No. 2);

j) Met, Ala, Pro, Ser, Thr or Val at position 285 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 294 of SEQ ID No. 2);

k) His or Asn at position 298 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 307 of SEQ ID No. 2);

l) Ile, Asn or Leu at position 326 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 335 of SEQ ID No. 2);

m) Met at position 359 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 368 of SEQ ID No. 2);

n) Tyr at position 372 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 381 of SEQ ID No. 2);

o) Ser at position 383 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 392 of SEQ ID No. 2);

p) Tyr at position 410 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 419 of SEQ ID No. 2);

q) Asp, Phe, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 412 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 421 of SEQ ID No. 2);

r) Ala, Met, Pro or Thr at position 413 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 422 of SEQ ID No. 2);

s) Ala, Ile or Val at position 415 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 424 of SEQ ID No. 2);

t) Ile, Pro, Arg, Als, Gly, Lys, Asn or Gln at position 416 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 425 of SEQ ID No. 2);

u) Phe, Thr, Val, Ala, Gln or Ser at position 417 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 426 of SEQ ID No. 2);

v) Met, Gln, Phe, Val, Phe or Leu at position 422 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 431 of SEQ ID No. 2);

w) Ala, Cys, Gly or Thr at position 219 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 228 of SEQ ID No. 2);

x) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 239 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 248 of SEQ ID No. 2);

y) Ala, Ile, Met or Val at position 261 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 270 of SEQ ID No. 2);

z) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 262 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 271 of SEQ ID No. 2);

aa) His at position 370 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 379 of SEQ ID No. 2);

bb) Arg at position 418 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 427 of SEQ ID No. 2).

[0063] In another embodiment, of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 26 [Triticum aestivum / wheat], wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys,Gln, Arg, Ser, Thr, Val, Tyr, Ile, Leu or Met at position 237 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 250 of SEQ ID No. 2), preferably Ala;
b) Asp, Glu, Lys, Leu, Asn, Pro, Arg or Ser, Gly, His or Trp at position 238 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Val or Tyr or Thr at position 239 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 252 of SEQ ID No. 2), preferably Tyr;
d) Ala, His, Gln, Val Trp, Ile, Leu or Met at position 240 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val or Met at position 252 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val, Tyr, Ala, Ile or Lys at position 255 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 256 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 267 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 280 of SEQ ID No. 2);
i) Leu, Val, Ala, Phe, Gly, Met, Arg or Ser at position 280 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 293 of SEQ ID No. 2);
j) Met, Ala, Pro, Ser, Thr or Val at position 281 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 294 of SEQ ID No. 2);
k) His or Asn at position 294 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 307 of SEQ ID No. 2);
l) Ile, Met or Asn at position 322 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
m) Met at position 355 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 368 of SEQ ID No. 2);
n) Tyr at position 368 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 381 of SEQ ID No. 2);
o) Ser at position 379 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 392 of SEQ ID No. 2);
p) Tyr at position 406 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 419 of SEQ ID No. 2);
q) Asp, Phe, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 408 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 421 of SEQ ID No. 2);
r) Ala, Met, Pro or Thr at position 409 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 422 of SEQ ID No. 2);
s) Ala, Ile or Val at position 411 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 424 of SEQ ID No. 2);
t) Ile, Pro, Arg, Ala, Gly, Lys, Asn or Gln at position 412 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 425 of SEQ ID No. 2);
u) Phe, Thr or Val, Ala, Gln or Ser at position 413 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 426 of SEQ ID No. 2);
v) Met, Gln, Phe, Leu or Val at position 418 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 431 of SEQ ID No. 2);
w) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 215 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 235 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Met or Val at position 257 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 270 of SEQ ID No. 2);
z) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 258 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 271 of SEQ ID No. 2);
aa) His at a position at position 366 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 379 of SEQ ID No. 2);
bb) Arg at position 414 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 427 of SEQ ID No. 2).

[0064] In another embodiment, of the isolated nucleic acid of the invention, said HPPD protein comprises the amino acid sequence of SEQ ID No. 2 [Arabidopsis thaliana], wherein the resulting amino acid sequence comprises at least one amino acid selected from

(a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val, Tyr, Ile, Leu or Met at position 250 of the amino acid sequence of SEQ ID No. 2;
(b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg, Ser, Gly, His or Trp at position 251 of the amino acid sequence of SEQ ID No. 2;
(c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Tyr or Thr at position 252 of the amino acid sequence of SEQ ID No. 2;
(d) Ala, His, Gln, Val, Trp, Ile, Leu or Met at position 253 of the amino acid sequence of SEQ ID No. 2;
(e) Val or Met at a position at position 265 of the amino acid sequence of SEQ ID No. 2;
(f) Leu, Gln, Arg, Val, Tyr, Ile, Lys or Met at position 268 of the amino acid sequence of SEQ ID No. 2;
(g) Ala or Thr at position 269 of the amino acid sequence of SEQ ID No. 2;
(h) Ala, Ile, Asn, Thr or Val at position 280 of the amino acid sequence of SEQ ID No. 2;
(i) Gln, Val, Ala, Phe, Gly, Met, Arg or Ser at a in an HPPD protein, said position corresponding to position 293 of the amino acid sequence of SEQ ID No. 2;
(j) Met, Ala, Pro, Ser, Thr or Val at position 294 of the amino acid sequence of SEQ ID No. 2;
(k) His or Asn at position 307 of the amino acid sequence of SEQ ID No. 2;
(l) Ile, Asn or Leu at position 335 of the amino acid sequence of SEQ ID No. 2;
(m) Met at position 368 of the amino acid sequence of SEQ ID No. 2;
(n) Tyr at position 381 of the amino acid sequence of SEQ ID No. 2;
(o) Ser at position 392 of the amino acid sequence of SEQ ID No. 2;
(p) Tyr at position 419 of the amino acid sequence of SEQ ID No. 2;
(q) Asp, Phe, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at position 421 of the amino acid sequence of SEQ ID No. 2 ;
(r) Ala, Met, Pro or Thr at position 422 of the amino acid sequence of SEQ ID No. 2;
(s) Ala, Ile or Val at position 424 of the amino acid sequence of SEQ ID No. 2;
(t) Ile, Pro, Arg, Ala, Gly, Lys, Asn or Gln at position 425 of the amino acid sequence of SEQ ID No. 2;
(u) Phe, Thr, Val, Ala, Gln or Ser at position 426 of the amino acid sequence of SEQ ID No. 2;
(v) Met, Gln, Val, Phe or Leu position 431 of the amino acid sequence of SEQ ID No. 2;
(w) Ala, Cys, Gly or Thr at position 228 of the amino acid sequence of SEQ ID No. 2;
(x) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 248 of the amino acid sequence of SEQ ID No. 2;
(y) Ala, Ile, Met or Val at position 270 of the amino acid sequence of SEQ ID No. 2;
(z) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 271 of the amino acid sequence of SEQ ID No. 2;
(aa) His at position 379 of the amino acid sequence of SEQ ID No. 2; or
(bb) Arg at position 427 of the amino acid sequence of SEQ ID No. 2.

[0065] In a further embodiment of the nucleic acid of the invention, in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises (a) Glu, Ser or Tyr at position 252; (b) Val or Ala at position 269; (c) Pro, Val or Ala at position 280; (d) Asp, Lys or Asn at position 421; and (e) Gly or Ala at postion 422. These positions correspond to amino acid sequence of SEQ ID No 2.

[0066] In a further embodiment of the nucleic acid of the invention, in said mutated HPPD protein at least two amino acids have been replaced.

[0067] An isolated nucleic acid comprising a nucleotide sequence encoding a mutated HPPD protein,
wherein said mutated HPPD protein has HPPD activity,
wherein in said mutated HPPD protein at least one amino acid at position 228, 248, 270, 271, 379 and/or 427 has been replaced by another amino acid.

[0068] In an alternative embodiment of the nucleic acid of the invention having at least one amino acid at position 228, 248, 270, 271, 379 and/or 427 deleted or replaced by another amino acid as defined above, said mutated HPPD protein comprises

a) a His at a position in an HPPD protein, said position corresponding to position 226 of the amino acid sequence of SEQ ID No. 2;
b) a Ser at a position in an HPPD protein, said position corresponding to position 267 comprising the amino acid sequence of SEQ ID No. 2 or at a position corresponding thereto in a different HPPD enzyme;
c) an Asn at a position in an HPPD protein, said position corresponding to position 282 of the amino acid sequence of SEQ ID No. 2;
d) a His at a position in an HPPD protein, said position corresponding to position 308 of the amino acid sequence of SEQ ID No. 2;

e) a Tyr at a position in an HPPD protein, said position corresponding to position 342 of the amino acid sequence of SEQ ID No. 2;
f) a Glu at a position in an HPPD protein, said position corresponding to position 394 of the amino acid sequence of SEQ ID No. 2;
g) a Gly at a position in an HPPD protein, said position corresponding to position 420 of the amino acid sequence of SEQ ID No. 2; and
h) an Asn at a position in an HPPD protein, said position corresponding to position 423 of the amino acid sequence of SEQ ID No. 2.

[0069] In another embodiment of the isolated nucleic acid as defined above, in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence has at least one selected from

a. Ala, Cys, Gly, Thr or Val at a position in an HPPD protein, said position corresponding to position 228 of the amino acid sequence of SEQ ID No. 2;
b. Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 248 of the amino acid sequence of SEQ ID No. 2;
c. Ala, Ile, Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 270 of the amino acid sequence of SEQ ID No. 2;
d. Ala, Glu, Hils, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 271 of the amino acid sequence of SEQ ID No. 2;
e. His or Gln at a position in an HPPD protein, said position corresponding to position 379 of the amino acid sequence of SEQ ID No. 2; and
f. Leu or Arg at a position in an HPPD protein, said position corresponding to position 427 of the amino acid sequence of SEQ ID No. 2.

[0070] In another embodiment of the isolated nucleic acid as defined above, in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence has at least one selected from

a. Val or Thr at a position in an HPPD protein, said position corresponding to position 228 of the amino acid sequence of SEQ ID No. 2;
b. Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 270 of the amino acid sequence of SEQ ID No. 2;
c. Ala or Ser at a position in an HPPD protein, said position corresponding to position 271 of the amino acid sequence of SEQ ID No. 2,
d. Gln at a position in an HPPD protein, said position corresponding to position 379 of the amino acid sequence of SEQ ID No. 2; and
e. Leu at a position in an HPPD protein, said position corresponding to position 427 of the amino acid sequence of SEQ ID No. 2.

[0071] In another embodiment of the nucleic acid as defined above, said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD (also called HPPD inhibitor herbicide).

[0072] In another embodiment, the present invention relates to a protein encoded by the isolated nucleic acid of the invention.

[0073] In a further embodiment, the present invention relates to a chimeric gene comprising a coding sequence comprising the nucleic acid of the invention operably linked to a plant-expressible promoter and optionally a transcription termination and polyadenylation region.

[0074] As a regulatory sequence which functions as a promoter in plant cells and plants, use may be made of any promoter sequence of a gene which is naturally expressed in plants, in particular a promoter which is expressed especially in the leaves of plants, such as for example "constitutive" promoters of bacterial, viral or plant origin, or "light-dependent" promoters, such as that of a plant ribulose-biscarboxylase/oxygenase (RuBisCO) small subunit gene, or any suitable known promoter-expressible which may be used. Among the promoters of plant origin, mention will be made of the histone promoters as described in EP 0 507 698 A1, the rice actin promoter (US 5,641,876), or a plant ubiquitin promoter (US 5,510,474). Among the promoters of a plant virus gene, mention will be made of that of the cauliflower mosaic virus (CaMV 19S or 35S, Sanders et al. (1987), Nucleic Acids Res. 15(4):1543-58.), the circovirus (AU 689 311) or the Cassava vein mosaic virus (CsVMV, US 7,053,205).

[0075] In one embodiment of this invention, a promoter sequence specific for particular regions or tissues of plants can be used to express the HPPD proteins of the invention, such as promoters specific for seeds (Datla, R. et al., 1997, Biotechnology Ann. Rev. 3, 269-296), especially the napin promoter (EP 255 378 A1), the phaseolin promoter, the glutenin promoter, the helianthinin promoter (WO 92/17580), the albumin promoter (WO 98/45460), the oleosin promoter (WO 98/45461), the SAT1 promoter or the SAT3 promoter (PCT/US98/06978).

[0076] Use may also be made of an inducible promoter advantageously chosen from the phenylalanine ammonia lyase (PAL), HMG-CoA reductase (HMG), chitinase, glucanase, proteinase inhibitor (PI), PR1 family gene, nopaline synthase (nos) and vspB promoters (US 5 670 349, Table 3), the HMG2 promoter (US 5 670 349), the apple beta-galactosidase (ABG1) promoter and the apple aminocyclopropane carboxylate synthase (ACC synthase) promoter (WO 98/45445).

[0077] According to the invention, use may also be made, in combination with the promoter, of other regulatory sequences, which are located between the promoter and the coding sequence, such as transcription activators ("enhancers"), for instance the translation activator of the tobacco mosaic virus (TMV) described in Application WO 87/07644, or of the tobacco etch virus (TEV) described by Carrington & Freed 1990, J. Virol. 64: 1590-1597, for example, or introns such as the adh1 intron of maize or intron 1 of rice actin.

[0078] As a regulatory terminator or polyadenylation sequence, use may be made of any corresponding sequence of bacterial origin, such as for example the nos terminator of *Agrobacterium tumefaciens,* of viral origin, such as for example the CaMV 35S terminator, or of plant origin, such as for example a histone terminator as described in published Patent Application EP 0 633 317 A1.

[0079] A method of obtaining a mutated HPPD protein capable of modulating the tolerance of a plant to at least one herbicide acting on HPPD, wherein said mutated HPPD protein has HPPD activity, the method comprising

i. providing an HPPD protein, said HPPD optionally comprising an amino acid sequence, wherein

  a) a His is present at a position in an HPPD protein, said position corresponding to position 226 of the amino acid sequence of SEQ ID No. 2;
  b) a Ser is present at a position in an HPPD protein, said position corresponding to position 267 of the amino acid sequence of SEQ ID No. 2;
  c) an Asn is present at a position in an HPPD protein, said position corresponding to position 282 of the amino acid sequence of SEQ ID No. 2;
  d) a His is present at a position in an HPPD protein, said position corresponding to position 308 of the amino acid sequence of SEQ ID No. 2;
  e) a Tyr is present at a position in an HPPD protein, said position corresponding to position 342 of the amino acid sequence of SEQ ID No. 2;
  f) a Glu is present at a position in an HPPD protein, said position corresponding to position 394 of the amino acid sequence of SEQ ID No. 2;
  g) a Gly is present at a position in an HPPD protein, said position corresponding to position 420 of the amino acid sequence of SEQ ID No. 2; and
  h) an Asn is present at a position in an HPPD protein, said position corresponding to position 423 of the amino acid sequence of SEQ ID No. 2

ii. replacing at least one amino acid in said HPPD enzyme so that the resulting amino acid sequence has at least one selected from

  a. Ala, Asp, Glu, Phe, Gly, Lys,Gln, Arg, Ser, Thr, Val, Ile, Leu, Met or Tyr at a position in an HPPD protein, said position corresponding to position 250 of the amino acid sequence of SEQ ID No. 2;
  b. Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg, Gly, His, Tyr or Ser at a position in an HPPD protein, said position corresponding to position 251 of the amino acid sequence of SEQ ID No. 2;
  c. Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 2;
  d. Ala, Phe, His, Gln, Val, Ile, Leu, Met or Trp at a position in an HPPD protein, said position corresponding to position 253 of the amino acid sequence of SEQ ID No. 2;
  e. Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 265 of the amino acid sequence of SEQ ID No. 2;
  f. Leu, Gln, Arg, Val, Ala, Ile, Lys, Met or Tyr at a position in an HPPD protein, said position corresponding to position 268 of the amino acid sequence of SEQ ID No. 2;
  g. Ala, Thr or Val at a position in an HPPD protein, said position corresponding to position 269 of the amino acid sequence of SEQ ID No. 2;
  h. Ala, Ile, Asn, Pro, Thr or Val at a position in an HPPD protein, said position corresponding to position 280 of the amino acid sequence of SEQ ID No. 2;
  i. Leu, Gln, Ala, Phe, Gly, Met, Arg, Ser or Val at a position in an HPPD protein, said position corresponding to

position 293 of the amino acid sequence of SEQ ID No. 2;
j. Ile, ala, Pro, Ser, Thr, Val or Met at a position in an HPPD protein, said position corresponding to position 294 of the amino acid sequence of SEQ ID No. 2;
k. Gln, His or Asn at a position in an HPPD protein, said position corresponding to position 307 of the amino acid sequence of SEQ ID No. 2;
l. Ile, Met, Leu or Asn at a position in an HPPD protein, said position corresponding to position 335 of the amino acid sequence of SEQ ID No. 2;
m. Leu or Met at a position in an HPPD protein, said position corresponding to position 368 of the amino acid sequence of SEQ ID No. 2;
n. Phe or Tyr at a position in an HPPD protein, said position corresponding to position 381 of the amino acid sequence of SEQ ID No. 2;
o. Phe or Ser at a position in an HPPD protein, said position corresponding to position 392 of the amino acid sequence of SEQ ID No. 2;
p. Phe or Tyr at a position in an HPPD protein, said position corresponding to position 419 of the amino acid sequence of SEQ ID No. 2;
q. Asp, Phe, Lys, Asn, Ala, Cys, Glu, Gly, His, Ile, Leu, Met, Gln, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 421 of the amino acid sequence of SEQ ID No. 2;
r. Ala, Gly, Met, Pro or Thr at a position in an HPPD protein, said position corresponding to position 422 of the amino acid sequence of SEQ ID No. 2;
s. Ala, Phe, Ile or Val at a position in an HPPD protein, said position corresponding to position 424 of the amino acid sequence of SEQ ID No. 2 or;
t. Ile, Pro, Arg, Ala, Gly, Lys, Asn, Gln or Ser at a position in an HPPD protein, said position corresponding to position 425 of the amino acid sequence of SEQ ID No. 2;
u. Glu, Phe, Thr, Ala, Gln, Ser or Val at a position in an HPPD protein, said position corresponding to position 426 of the amino acid sequence of SEQ ID No. 2;
v. Ile, Met, Gln, Phe, Leu or Val at a position in an HPPD protein, said position corresponding to position 431 of the amino acid sequence of SEQ ID No. 2;
w. an amino acid deletion or replacement at least one position in an HPPD protein, said position corresponding to at least one of positions 228, 248, 270, 271, 379 and 427 of the amino acid sequence of SEQ ID No. 2;

iii. determining the inhibition of the resulting HPPD protein by at least one herbicide acting on HPPD;

wherein an inhibition of the resulting protein of less or more than that observed with a reference HPPD protein is indicative that the resulting protein is capable of modulating the tolerance of a plant to said herbicide.

[0080] It is to be understood that also the (more specific) amino acids and positions listed above for other embodiments, such as the nucleic acid of the invention, may be applied to the method of obtaining a mutated HPPD protein as described above.

[0081] In an alternative embodiment of the method of obtaining a mutated HPPD protein as described above, said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD.

[0082] Within the above method of obtaining in mutated HPPD protein, different herbicides acting on HPPD may be chosen. Accordingly, in another embodiment of the method of obtaining a mutated HPPD protein as described above, wherein said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD, the herbicide acting on HPPD is selected from triketones, or pyrazolinates, preferably tembotrione, mesotrione, topramezone or sulcotrione, bicyclopyrone, pyrasulfotole, pyrazolate, benzofenap and tefuryltrione, particularly tembotrione and such plants containing the HPPD of the invention have an agronomically acceptable tolerance to an HPPD inhibitor herbicide particularly to triketones, or pyrazolinates, preferably tembotrione, mesotrione, topramezone or sulcotrione, bicyclopyrone, pyrasulfotole, pyrazolate, benzofenap and tefuryltrione, particularly tembotrione.

[0083] In another embodiment, the present invention relates to a method of producing a transgenic plant comprising introducing into a said plant genome the nucleic acid of the present invention operably linked to a plant expressible promoter, the chimeric gene of the invention or a nucleic acid encoding the HPPD enzyme identified by the method of of claim 27 or 28.

[0084] In an alternative embodiment of the method of producing a transgenic plant as described above, the nucleic acid of the invention, wherein said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD, or a nucleic acid identified by the method of obtaining a mutated HPPD protein, wherein said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicie acting on HPPD, both operably linked to a plant expressible promoter, or the chimeric gene of the invention comprising a nucleic acid, wherein said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicie acting on HPPD, is introduced into said plant.

[0085] In another embodiment, the present invention relates to a plant cell comprising the isolated nucleic acid of the invention or the chimeric gene of the invention in its genetic information.

[0086] The present invention also relates to a plant, a part of a plant or plant tissue consisting essentially of the plant cells of the invention.

[0087] Furthermore, the present invention relates to a plant obtainable from the method of obtaining a mutated HPPD protein capable of modulating or increasing the tolerance of a plant to at least one herbicide acting on HPPD in all alternative aspects described above.

[0088] The plant of the present invention can be any plant. Non-limiting examples of plants of the invention include wheat, cotton, canola, rice, corn, soy bean, sorghum,canola, sunflower, tobacco, sugarbeet, cotton, maize, wheat, barley, rice, sorghum, tomato, mango, peach, apple, pear, strawberry, banana, melon, potato, carrot, lettuce, cabbage, onion, soya spp, sugar cane, pea, field beans, poplar, grape, citrus, alfalfa, rye, oats, turf and forage grasses, flax and oilseed rape, and nut producing plants. The present invention also relates to a seed of the plant of the invention. Furthermore, the invention relates to progeny of the plant of the invention or the seed of the invention.

[0089] In a further embodiment, the present invention relates to a method of modulating a plant's tolerance to at least one herbicide acting on HPPD comprising introducing the isolated nucleic acid of the invention operably linked to a plant expressible promoter or the chimeric gene of the invention into a plant's genome

[0090] In an alternative embodiment, the present invention relates to a method of increasing a plant's tolerance to at least one herbicide acting on HPPD or of obtaining a plant tolerant to an HPPD inhibitor herbicide comprising introducing the isolated nucleic acid of the invention, wherein said nucleic acid encodes a mutated HPPD protein which is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD, operably linked to a plant expressible promoter or the chimeric gene of the invention comprising a nucleic acid of the invention, wherein said nucleic acid encodes a mutated HPPD protein which is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD, into a plant's genome.

[0091] Furthermore, the present invention relates to a method for controlling weeds comprising spraying at least one herbicide acting on HPPD on or around a crop plant, wherein said crop plant comprises the nucleic acid of the present invention, wherein said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD, operably linked to a plant expressible promoter or the chimeric gene of the invention comprising the nucleic acid of the invention, wherein said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD. In alternative embodiment of the method of controlling weeds, the tolerance of said plant to at least one herbicie acting on HPPD is increased.

[0092] In addition, the present invention relates to the use of a chimeric gene of the invention or the nucleic acid of the invention operably linked to a plant expressible promoter for modulating the tolerance of a plant to at least one herbicide acting on HPPD.

[0093] In an alternative embodiment, the present invention relates to the use of a chimeric gene of the invention or the nucleic acid of the invention operably linked to a plant expressible promoter for increasing the tolerance of a plant to at least one herbicide acting on HPPD. In this embodiment of the invention, the chimeric gene used comprises the nucleic acid of the invention, wherein the mutated HPPD protein encoded thereby is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD. Alternatively, if a nucleic acid operably linked to a plant expressible promoter is used, said nucleic is chose that the mutated HPPD protein encoded thereby is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD.

[0094] The present invention also relates to the plant cell of the invention and the plant of the invention which may comprise a further useful trait as described further below.

[0095] While a number of herbicide-tolerant crop plants are presently commercially available, one issue that has arisen for many commercial herbicides and herbicide/crop combinations is that individual herbicides typically have incomplete spectrum of activity against common weed species. For most individual herbicides which have been in use for some time, populations of herbicide resistant weed species and biotypes have become more prevalent (see, e.g., Tranel and Wright (2002) Weed Science 50: 700-712; Owen and Zelaya (2005) Pest Manag. Sci. 61: 301-311). Transgenic plants which are resistant to more than one herbicide have been described (see, e.g., W02005/012515). However, improvements in every aspect of crop production, weed control options, extension of residual weed control, and improvement in crop yield are continuously in demand.

[0096] The HPPD protein or gene of the invention is advantageously combined in plants with other genes which encode proteins or RNAs that confer useful agronomic properties to such plants. Among the genes which encode proteins or RNAs that confer useful agronomic properties on the transformed plants, mention can be made of the DNA sequences encoding proteins which confer tolerance to one or more herbicides that, according to their chemical structure, differ from HPPD inhibitor herbicides, and others which confer tolerance to certain insects, those which confer tolerance to certain diseases, DNAs that encodes RNAs that provide nematode or insect control, etc...

[0097] Such genes are in particular described in published PCT Patent Applications WO 91/02071 and WO95/06128.

[0098] Among the DNA sequences encoding proteins which confer tolerance to certain herbicides on the transformed plant cells and plants, mention can be made of a bar or PAT gene or the *Streptomyces coelicolor gene* described in W02009/152359 which confers tolerance to glufosinate herbicides, a gene encoding a suitable EPSPS which confers tolerance to herbicides having EPSPS as a target, such as glyphosate and its salts (US 4,535,060, US 4,769,061, US 5,094,945, US 4,940,835, US 5,188,642, US 4,971,908, US 5,145,783, US 5,310,667, US 5,312,910, US 5,627,061, US 5,633,435), or a gene encoding glyphosate oxydoreductase (US 5,463,175).

[0099] Among the DNA sequences encoding a suitable EPSPS which confer tolerance to the herbicides which have EPSPS as a target, mention will more particularly be made of the gene which encodes a plant EPSPS, in particular maize EPSPS, particularly a maize EPSPS which comprises two mutations, particularly a mutation at amino acid position 102 and a mutation at amino acid position 106 (WO 2004/074443), and which is described in Patent Application US 6566587, hereinafter named double mutant maize EPSPS or 2mEPSPS, or the gene which encodes an EPSPS isolated from Agrobacterium and which is described by sequence ID No. 2 and sequence ID No. 3 of US Patent 5,633,435, also named CP4.

[0100] Among the DNA sequences encoding a suitable EPSPS which confer tolerance to the herbicides which have EPSPS as a target, mention will more particularly be made of the gene which encodes an EPSPS GRG23 from Arthrobacter globiformis, but also the mutants GRG23 ACE1, GRG23 ACE2, or GRG23 ACE3, particularly the mutants or variants of GRG23 as described in WO2008/100353, such as GRG23(ace3)R173K of SEQ ID No. 29 in WO2008/100353.

[0101] In the case of the DNA sequences encoding EPSPS, and more particularly encoding the above genes, the sequence encoding these enzymes is advantageously preceded by a sequence encoding a transit peptide, in particular the "optimized transit peptide" described in US Patent 5,510,471 or 5,633,448.

[0102] In WO 2007/024782, plants being tolerant to glyphosate and at least one ALS (acetolactate synthase) inhibitor are disclosed. More specifically plants containing genes encoding a GAT (Glyphosate-N-Acetyltransferase) polypeptide and a polypeptide conferring resistance to ALS inhibitors are disclosed. In US 6855533, transgenic tobacco plants containing mutated Arabidopsis ALS/AHAS genes were disclosed.

[0103] In US 6,153,401, plants containing genes encoding 2,4-D-monooxygenases conferring tolerance to 2,4-D (2,4-dichlorophenoxyacetic acid) by metabolisation are disclosed.

[0104] In US 2008/0119361 and US 2008/0120739, plants containing genes encoding Dicamba monooxygenases conferring tolerance to dicamba (3,6-dichloro-2-methoxybenzoic acid) by metabolisation are disclosed.

[0105] All the above mentioned herbicide tolerance traits can be combined with those performing HPPD tolerance which are subject matter of this invention.

[0106] Among the DNA sequences encoding proteins concerning properties of tolerance to insects, mention will more particularly be made of the Bt proteins widely described in the literature and well known to those skilled in the art. Mention will also be made of proteins extracted from bacteria such as *Photorhabdus* (WO 97/17432 & WO 98/08932).

[0107] Among such DNA sequences encoding proteins of interest which confer novel properties of tolerance to insects, mention will more particularly be made of the Bt Cry or VIP proteins widely described in the literature and well known to those skilled in the art. These include the Cry1 F protein or hybrids derived from a Cry1 F protein (e.g., the hybrid Cry1A-Cry1F proteins described in US 6,326,169; US 6,281,016; US 6,218,188, or toxic fragments thereof), the Cry1A-type proteins or toxic fragments thereof, preferably the Cry1Ac protein or hybrids derived from the Cry1Ac protein (e.g., the hybrid Cry1Ab-Cry1Ac protein described in US 5,880,275) or the Cry1Ab or Bt2 protein or insecticidal fragments thereof as described in EP451878, the Cry2Ae, Cry2Af or Cry2Ag proteins as described in WO02/057664 or toxic fragments thereof, the Cry1A.105 protein described in WO 2007/140256 (SEQ ID No. 7) or a toxic fragment thereof, the VIP3Aa19 protein of NCBI accession ABG20428, the VIP3Aa20 protein of NCBI accession ABG20429 (SEQ ID No. 2 in WO 2007/142840), the VIP3A proteins produced in the COT202 or COT203 cotton events (WO 2005/054479 and WO 2005/054480, respectively), the Cry proteins as described in WO01/47952, the VIP3Aa protein or a toxic fragment thereof as described in Estruch et al. (1996), Proc Natl Acad Sci U S A. 28;93(11):5389-94 and US 6,291,156, the insecticidal proteins from *Xenorhabdus* (as described in WO98/50427), *Serratia* (particularly from S. *entomophila)* or *Photorhabdus* species strains, such as Tc-proteins from Photorhabdus as described in WO98/08932 (e.g., Waterfield et al., 2001, Appl Environ Microbiol. 67(11):5017-24; Ffrench-Constant and Bowen, 2000, Cell Mol Life Sci.; 57(5):828-33). Also any variants or mutants of any one of these proteins differing in some (1-10, preferably 1-5) amino acids from any of the above sequences, particularly the sequence of their toxic fragment, or which are fused to a transit peptide, such as a plastid transit peptide, or another protein or peptide, is included herein.

[0108] The FIGURES show:

FIGURE1: Superpositon of the x-ray structure of HPPD from *Arabidopsis thaliana* (dark grey) and (a) *Pseudomonas fluorescens* (light grey), (b) *Streptomyces avermitilis,* (c) *Homo sapiens, (d) Rattus norvegicus.* The structures are shown as ribbon plot.

FIGURE2: Amino acids forming the binding site of (a) Arabidopsis thaliana, (b) *Pseudomonas fluorescens* (c) *Streptomyces avermitilis (d) Homo sapiens, and (e) Rattus norvegicus* (represented by bold lines). The core

of the HPPD protein is shown as C_{alpha} trace and the iron is marked.

FIGURE3: Brown test color in *Escherichia coli*

SEQUENCES LISTING

[0109]

SEQ ID No. 1: Nucleic acid sequence encoding Arabidopsis thaliana HPPD

SEQ ID No. 2: Protein encoded by SEQ ID No. 1

SEQ ID No. 3: Nucleic acid sequence encoding Oryza sativa HPPD

SEQ ID No. 4: Protein encoded by SEQ ID No. 3

SEQ ID No. 5: Nucleic acid sequence encoding Zea mays HPPD

SEQ ID No. 6: Protein encoded by SEQ ID No. 5

SEQ ID No. 7: Nucleic acid sequence encoding Avena sativa HPPD

SEQ ID No. 8: Protein encoded by SEQ ID No. 7

SEQ ID No. 9: Nucleic acid sequence encoding Pseudomonas fluorescens HPPD

SEQ ID No. 10: Protein encoded by SEQ ID No. 9

SEQ ID No. 13: Nucleic acid sequence encoding Synechococcus sp. HPPD

SEQ ID No. 14: Protein encoded by SEQ ID No. 13

SEQ ID No. 15: Nucleic acid sequence encoding Blepharsima japonicum HPPD

SEQ ID No. 16: Protein encoded by SEQ ID No. 15

SEQ ID No. 17: Nucleic acid sequence encoding Rhodococcus RHA1 isolate ro0341 HPPD

SEQ ID No. 18: Protein encoded by SEQ ID No. 17

SEQ ID No. 19: Nucleic acid sequence encoding Picrophilus torridus HPPD

SEQ ID No. 20: Protein encoded by SEQ ID No. 19

SEQ ID No. 21: Nucleic acid sequence encoding Kordia algicida HPPD

SEQ ID No. 22: Protein encoded by SEQ ID No. 21

SEQ ID No. 23: Nucleic acid sequence encoding Sorghum bicolor HPPD

SEQ ID No. 24: Protein encoded by SEQ ID No. 23

SEQ ID No. 25: Nucleic acid sequence encoding Triticum aestivum HPPD

SEQ ID No. 26: Protein encoded by SEQ ID No. 25

SEQ ID No. 27: Nucleic acid sequence encoding Hordeum vulgare HPPD

SEQ ID No. 28: Protein encoded by SEQ ID No. 27

SEQ ID No. 29: Nucleic acid sequence encoding Rhodococcus RHA1 isolate ro0240 HPPD

SEQ ID No. 30: Protein encoded by SEQ ID No. 29

SEQ ID No. 31: Nucleic acid sequence encoding Arabidopsis thaliana wild type HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 32: Protein encoded by SEQ ID No. 31

SEQ ID No. 33: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 34: Protein encoded by SEQ ID No. 33,

SEQ ID No. 35: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 36: Protein encoded by SEQ ID No. 35,

SEQ ID No. 37: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 38: Protein encoded by SEQ ID No. 37,

SEQ ID No. 39: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 40: Protein encoded by SEQ ID No. 39,

SEQ ID No. 41: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 42: Protein encoded by SEQ ID No. 41,

SEQ ID No. 43: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 44: Protein encoded by SEQ ID No. 43,

SEQ ID No. 45: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 46: Protein encoded by SEQ ID No. 45

SEQ ID No. 47: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 48: Protein encoded by SEQ ID No. 47

SEQ ID No. 49: Nucleic acid sequence encoding mutant HPPD polypeptide, plus containing at the 5' end a nucleic acid encoding an alanine and 6 histidine amino acids

SEQ ID No. 50: Protein encoded by SEQ ID No. 49,

[0110] The Examples illustrate the invention

Example1:

[0111] A mutation of strictly conserved amino acids leads to an inactive protein.

[0112] The point mutants S267A (SEQ ID No. 34) in *A.thaliana* and N282A (SEQ ID No. 36) in *A.thaliana* are inactive. The amino acid position given are referring to the position of SEQ ID No. 2.

[0113] Mutant HPPD polypeptides of the presenting invention have amino acids changes at one or more positions relative to the starting wild type sequence from which they are derived.

[0114] The DNA sequence SEQ ID No. 2 encoding the wild HPPD protein from Arabidopsis thaliana (1335 bp; Genebank AF047834; WO 96/38567) was cloned into the vector pSE420(RI)NX (modified from the the cloning and expression vector pSE420(RI)NX (5261 bp) is based on the plasmid pSE420 by Invitrogen (Karlsruhe, Germany)). At the 5' end, directly downstream to the ATG was inserted a nucleic acid sequence coding for an alanine amino acid and a nucleic acid sequence encoding a N-terminal HIS6-Tag (6x HIS, encoded by: cat cat cat cac cat cat). The resulting sequence is presented as SEQ ID No. 31. Upstream to the ATG, two additional cysteine base pairs were added in order to obtain a sequence corresponding to the recognition site of the restriction enzyme NcoI and downstream to the stop codon the sequences corresponding to the recognition site of the restriction enzyme XbaI were added. The resulting plasmid was then used to transform E. Coli cells BL21 (DE3) with 50pg/ml kanamycin or 100μg/ml carbenicillin selection as described in European patent applications "EP09015984.9"; EP09015985.6"; EP 09015986.4" EP 09015987.2"; and EP09015988.0" all filed on 23. December 2009.

[0115] Quick test of the activity of HPPD protein: Production of brown color

[0116] Colorimetric Screening Test for Active HPPD Enzymes:

A YT-broth-type culture medium with 1% agarose, 5mM L-Tyrosine and 42mM Succinate, which contains the selection agent for the vector pSE420 is poured into deep well plates. E.coli culture in the exponentional growth phase which contains the vector pSE420-HPPDx (any gene coding for a putative HPPD enzyme/protein) is applied to each well. After 16 hours at 37°C, the wells which do not contain the culture medium, those which have been seeded with an E. coil culture containing the empty vector pSE420 are transparent, or those which have been seeded with an E.

coli culture containing a vector pSE420 containing a gene coding for an inactive HPPD are transparent, while the wells seeded with an E. coli culture containing the vector pSE420-HPPD coding for active HPPD are brown. It has been previously demonstrated that this test refelects the HPPD activity, whatever the orgin of this activity, and allows the identification of HPPD activities (US 6,768,044).

As it can be seen on Figure 3, the culture from bacteria containing the gene coding for the mutant HPPD did not develop a brown color while the one containing the gene coding of the wild type HPPD developed a strong brown color reflecting the activity of the HPPD enzymes. It can be concluded that the two HPPD mutants are not able to convert HPP into homogentisate. The two HPPD mutants are inactive.

One can conclude that the amino acid positions 267 and 282 (referring to position in SEQ ID No. 2) are essential for HPPD activity.

[0117] The expression of the HPPD protein was then done as following.

[0118] Overnight cultures grown at 37°C were used to inoculate LB media at a ratio 1:100. Cells were allowed to grow until OD reached 0.5, then expression was initiated from the trp-lac (trc) promoter by induction with 1 mM IPTG which binds to the *lac* repressor and causes its dissociation from the *lac* operon. Expression was carried out over 15 h at 28 °C.

[0119] To prepare the pre-starter culture, 2 mL of TB medium (100 $\mu g*mL^{-1}$ carbenicillin) were inoculated with 50 μL of an *E. coli* K-12 BL21 glycerol stock. The pre-starter culture was incubated at 37 °C with shaking at 140 rpm for 15 h. 200μl of the pre-starter culture was used to initiate the starter culture (5mL TB supplement with 100 $\mu g*L^{-1}$), which was incubated 3 h at 37°C.

[0120] To prepare the main culture, 400 mL of TB medium (100 $\mu g*mL^{-1}$ carbenicillin) were inoculated with 4 mL of the starter culture. This starter culture was incubated at 37 °C with shaking at 140 rpm until OD_{600} 0.5 was reached. Then recombinant protein expression was induced with 400 μl of 1 M IPTG solution. The cells were allowed to grow for an additional hour under these conditions, then the temperature was lowered to 28°C and the culture was shaken at 140 rpm for 15 h. Cells were harvested by centrifugation at 6000 x g for 15 min at 4 °C. Then cell pellets were stored at -80 °C.

[0121] Isolation and purification of His_6-AtHPPD in native form

Lysis of cells

[0122] Cells were lysed using Lysozyme, an enzyme that cleaves the 1,4-β-linkages between N-acetylmuramic acid and N-acetyl-D-glucosamine residues in peptidoglycan which forms the bacterial cell wall. Cell membranes were then disrupted by the internal pressure of the bacterial cell. In addition, the lysis buffer contained Benzonase® Nuclease, an endonuclease that hydrolyzes all forms of DNA and RNA without damaging proteins and thereby largely reduces viscosity of the cell lysate. Lysis under native conditions was carried out on ice.

[0123] For purification of His$_6$-tagged proteins the QIA*express*® Ni-NTA Fast Start Kit was used following the user manual instruction.

[0124] Purification of His$_6$-tagged proteins by immobilized metal ion affinity chromatography (IMAC)

[0125] The cleared cell lysate (10 mL) obtained after centrifugation of the lysis reaction was loaded onto a Ni-NTA Fast Start Column from the QIA*express*® Ni-NTA Fast Start Kit (Qiagen, Hilden, Germany) and purification was carried out according to the instruction manual. The His$_6$-tagged protein was eluted with 2.5 mL of elution buffer.

Desalting of HPPD solutions by gel filtration

[0126] HPPD solutions eluted from a Ni-NTA Fast Start Column with 2.5 mL of elution buffer were applied to a Sephadex G-25 PD-10 column (GE Healthcare, Freiburg, Germany) following the user manual instruction. After the whole sample had entered the gel bed, elution was performed with 3.5 mL of storage buffer. The HPPD solutions eluted from the desalting column were frozen at -80 °C in 1 mL aliquots.

[0127] Determination of HPPD protein concentration using the Bradford protein assay Protein concentration was determined using the standard Bradford assay (Bradford, (1976), Anal Biochem 72: 248-254).

Determination of purity of HPPD solutions using SDS-PAGE

[0128] The integrity of the eluted protein was checked by SDS-PAGE protein gel electrophoresis using the gel NuPAGE® Novex 4-12 % Bis-Tris Gels (Invitrogen, Karlsruhe, Germany), approximately 10 μg of protein were loaded. 10 μL of Laemmli Sample Buffer was added to 1-10 μL of protein solution and the mixture was incubated at 90 °C for 10 min. After short centrifugation step, the whole mixture was loaded into a slot of an SDS gel previously fixed in a XCell *SureLock*™ Novex Mini-Cell gel chamber filled with NuPAGE® MOPS SDS Running Buffer (diluted from the 20 x-solution with ddH$_2$O). A voltage of 150 was then applied to the gel chamber for 1 h. For staining of protein bands, the gel was immersed in Coomassie Brilliant Blue R-250 Staining Solution. For destaining of the polyacrylamide gel, it was immersed in Coomassie Brilliant Blue R-250 Destaining Solution until protein bands appear blue on a white gel.

[0129] The HPPD activity was checked by the standard spectrophotmetric assay (method extensively described in WO 2009/144079)

[0130] In this content, pI$_{50}$-value means the log value of the concentration of inhibitor necessary to inhibit 50% of the enzyme activity in molar concentration.

[0131] pI$_{50}$-values for HPPD inhibitors were determined from dose-response plots of HPPD activity versus inhibitor concentration using the assay extensively described in WO 2009/144079 at 2 mM fixed HPP concentration and 3 minutes fixed incubation time using the ID Business Solutions Ltd. XLfit software suite.

Table 7: Determination of pI50 HPPD enzymes (*Arabidopsis thaliana* wild type HPPD “SEQ ID No. 32”, the mutants S267A (SEQ ID No. 34) and N282A (SEQ ID No. 36)” and the tolerance to the several listed below HPPD inhibitors tembotrione, diketonitrile, mesotrione, bicyclopyrone, pyrasulfotole, sulcotrione, pyrazolate, tefuryltrione, and benzofenap. The symbol “>” means that the value was far higher than the one indicated but could not be precisely calculated within in the range of concentration of inhibitor tested ($2.5x10^{-6}$, $5.0x10^{-6}$, $1.0x10^{-5}$, $2.5x10^{-5}$, $6.3x10^{-5}$, and $2.5x10^{-4}$M).

	Bicyclopyrone	Benzofenap	Diketonitrile	Mesotrione
WT (SEQ ID No. 32)	5.2	>5.6	>5.6	>5.6
S267A (SEQ ID No. 34)	nd - la (P)	nd - la (P)	nd - la (P)	nd - la (P)
N282A (SEQ ID No. 36)	nd - la (P)	nd - la (P)	nd - la (P)	nd - la (P)

	Pyrasulfotole	Pyrazolate	Sulcotrione	Tefuryltrione	Tembotrione
WT (SEQ ID No. 32)	5.4	5.4	>5.6	>5.6	>5.6
S267A (SEQ ID No. 34)	nd - la (P)	nd - la (P)	nd - la (P)	nd - la (P)	nd - la (P)
N282A (SEQ ID No. 36)	nd - la (P)	nd - la (P)	nd - la (P)	nd - la (P)	nd - la (P)

[0132] As previously demonstrated, the 2 protein mutants are not able to convert HPP into Homogentisate, confirming that the 2 mutant proteins are inactive. It confirms the hypothesis that the position 267 and 282 (referring to position in SEQ ID No. 2) are absolutely essential for obtaining an active HPPD

Example 2: Single point mutants displayed increased tolerance to HPPD inhibitor herbicides:

[0133] Kinetic characterization and evaluation of tolerance to HPPD inhibitors of HPPD enzyme "SEQ ID No. 32".

[0134] The HPPD activity was checked by the standard spectrophotmetric assay (method extensively described in WO 2009/144079)

Determination of HPPD in vitro kinetic properties

[0135] K_m, V_{max}, and k_{cat} values for different HPPD enzyme preparations and K_i, K_1=K_{on}, and K_{-1}=K_{off} for different HPPD inhibitors were determined using a HPLC assay for measurements of HPPD activity. The assay mixtures contained in a volume of 1 ml 150 mM Tris-HCl buffer at pH 7.8, 10 mM sodium ascorbate, 650 units of bovine catalase (Sigma C30 (Sigma-Aldrich, Munich,Germany), 34 mg protein/ml, 23,000 units/mg), and appropriate amounts of HPP, purified HPPD enzyme and HPPD inhibitors. For K_m, V_{max}, and k_{cat} value determination HPP concentrations in the assay mixture were varied between 10 and 400 µM. For K_i, K_1=K_{on}, and K_{-1}=K_{off} value determination 2 mM HPP was used. All assays were started by the addition of HPPD enzyme to the assay mixture and stopped at a series of times between 0 and 240 s by addition of 200 µl of the reaction mixture to reaction assay tubes containing 20 µl 10% perchloric acid. Precipitated protein was pelleted by a 5 minute centrifugation at 10,000 g. 100 µl of the supernatant were loaded onto a 250 x 4mm Knauer (Berlin, Germany) Eurospher 100-5 C18-column equilibrated with 10% methanol, 0.1 % trifluoroacetic acid (buffer A). The column was eluted, also at 1.5 ml/min, using a 4 minute wash with buffer A, followed by a 3 min wash with 95% methanol and by a further 2 minute wash with buffer A. The elution of HGA (homogentisic acid) and HPP (hydroxyphenylpyruvate) was monitored at 292 nm. HGA elutes at around 5 minutes and HPP elutes later. A standard set of concentrations of HGA were used to provide a standard curve in order to calibrate the 292 nm absorbance of the HGA peak versus HGA concentration. For K_m and V_{max} value determinations the initial rates of the HPPD reaction at different substrate concentrations were determined from plots of HGA formed versus time and fitted to the Michaelis-Menten equation for unireactant enzymes using the ID Business Solutions Ltd. (www.idbs.com) XLfit software suite. For the determination of K_i, K_1=K_{on}, and K_{-1}=K_{off} values the time-courses of the HPPD reaction at different inhibitor concentrations were fitted to the equations for Mechanism A, competitive inhibition, for tight-binding inhibitors (Cha, S. (1975) Tight-binding inhibitors - I. Kinetic behaviour. Biochemical Pharmacology 24, 2177-2185) using the ID Business Solutions Ltd. XLfit software suite

Table 8

[0136] Protein SEQ ID No. 32 consists of protein SEQ ID No. 2 with an insertion of one amino acid Ala and six amino acids His directly behind the first methionine.

[0137] Kinetic characterization of HPPD enzymes *(Arabidopsis thaliana* "SEQ ID No. 32" and the respective tolerance to the HPPD inhibitors tembotrione and diketonitrile. In below given table1, "K_m" (Michaelis-Menten constant) means the kinetic parameter that is used to characterise an enzyme, and it is defined as the concentration of substrate that permits half maximal rate of the reaction. K_m is further defined as the substrate concentration at which the reaction rate reaches half of its maximum value (V_{max}/2) where Vmax has the meaning of being the maximum velocity of the reaction. K_{on}=K_1 equals the association rate constant of the enzyme-substrate binding and K_{off}=K_{-1} equals the rate constant of the enzyme-inhibitor complex dissociation. Ki defines the inhibition constant.

	HPP		Tembotrione			Diketonitrile		
	K_m (µM)	V_{max} (µM)	k_1 (M^{-1} s^{-1})	k_{-1} (s^{-1})	K_1 (µM)	k_1 (M^{-1}) (s^{-1})	k_{-1} (s^{-1})	k_1 (µM)
SEQ ID No. 32	6.3	1.2	2.3E+05	3.5E-03	0.015	6.1E+05	1.1 E-02	0.018

[0138] The kinetic parameters K_m and V_{max} of the plant HPPD "SEQ ID No. 32" summarized in Table 8 are well in the range of the specific activities measured from purified plant HPPD as for example for the carrot HPPD (Garcia et al. 2000, Biochemistry, 39, 7501-7507). The Arabidopsis thaliana HPPD is also sensitive in the smimilar range as the carrot HPPD to diketonitrile. It is the first time, that the kinetic parameter of Arabidopsis thaliana HPPD in presence of tembotrione are measured and being in a comparable range as the one measured in presence of the HPPD inhibitor diketonitrile.

[0139] Determination of HPPD activity in presence of several HPPD inhibitors

[0140] In this content, pI_{50}-value means the log value of the concentration of inhibitor necessary to inhibit 50% of the enzyme activity in molar concentration.

[0141] pI_{50}-values for HPPD inhibitors were determined from dose-response plots of HPPD activity versus inhibitor concentration using the assay extensively described in WO 2009/144079 at 2 mM fixed HPP concentration and 3 minutes fixed incubation time using the ID Business Solutions Ltd. XLfit software suite.

Table 9: Determination of pI50 HPPD enzymes (*Arabidopsis thaliana* "SEQ ID No. 32" and some Arabidopsis HPPD single point mutants "SEQ ID No. 35, SEQ ID No. 40, SEQ ID No. 42, SEQ ID No. 44, SEQ ID No. 46, SEQ ID No. 48, and SEQ ID No. 50") and their respective tolerance to the several listed below HPPD inhibitors tembotrione, diketonitrile, mesotrione, bicyclopyrone, pyrasulfotole, sulcotrione, pyrazolate, tefuryltrione, and benzofenap. The symbol ">" means that the value was far higher than the one indicated but could not be precisely calculated within in the range of concentration of inhibitor tested ($2.5x10^{-6}$, $5.0x10^{-6}$, $1.0x10^{-5}$, $2.5x10^{-5}$, $6.3x10^{-5}$, and $2.5x10^{-4}$M).

	Bicyclopyrone	Benzofenap	Diketonitrile	Mesotrione	Pyrasulfotole
SEQ ID No. 32	5.2	>5.6	>5.6	>5.6	5.4
E252S (SEQ ID No. 36)	4.3	5.2	4.9	5.3	4.3
V269A (SEQ ID No. 40)	4.3	5.2	5.2	5.2	4.4
P280A SEQ ID No. 42	4.3	5.2	5.2	5.3	4.4
L368M SEQ ID No. 44	4.5	>5.6	5.6	5.4	5.0
K421I SEQ ID No. 46	4.2	5.1	5.0	5.2	4.3
K421Q SEQ ID No. 48	4.7	>5.6	>5.6	>5.6	4.8
K421V SEQ ID No. 50	4.2	5.2	5.1	5.3	4.4

	Pyrazolat	Sulcotrione	Tefuryltrione	Tembotrione
SEQ ID No. 32	5.4	>5.6	>5.6	>5.6
E252S (SEQ ID No. 35)	4.7	5.1	5.2	5.5
V269A (SEQ ID No. 40)	4.4	5.0	5.4	>5.6
P280A SEQ ID No. 42	4.7	5.0	5.5	>5.6
L368M SEQ ID No. 44	4.9	5.2	>5.6	>5,6
K421I SEQ ID No. 46	4.5	5.0	5.2	5.6
K421Q SEQ ID No. 48	5.0	>5.6	>5.6	>5.6
K421V SEQ ID No. 50	4.5	5.1	5.4	>5.6

[0142] Measurements show that the pl50 in case of the point mutants is reduced compared to the wild-type protein.

[0143] In Table 9, it can be clearly seen that the HPPD mutants are all affected in their tolerance to at least one HPPD inhibitors and some to several HPPD inhibitors. All the tested mutants are more active (do show an increased tolerance concerning the various applyied HPPD inhibitors) in the presence of at least one of the selected HPPD inhibitors, therefore the mutant enzyme-inhibitor complex should be less stable the wild-type enzyme-inhibitor complex. It can be concluded that the positions 252, 269, 280, 368 and 421 (reference taken in SEQ ID No. 2) are all important in the modulation of tolerance of HPPD enzyme to HPPD inhibitors.

SEQUENCE LISTING

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<120> HPPD variants and methods of use

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Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val Arg Ala Val Ala Ile
    130                 135                 140


Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile Ser Val Ala Asn Gly
145                 150                 155                 160


Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn Glu Ala Val Thr Ile
                165                 170                 175


Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu Arg Tyr Val Ser Tyr
            180                 185                 190
```

```
Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu Pro Gly Phe Glu Arg
        195                 200                 205

Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr Gly Ile Arg Arg Leu
    210                 215                 220

Asp His Ala Val Gly Asn Val Pro Glu Leu Gly Pro Ala Leu Thr Tyr
225                 230                 235                 240

Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala Glu Phe Thr Ala Asp
                245                 250                 255

Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser Ala Val Leu Ala Ser
            260                 265                 270

Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu Pro Val His Gly Thr
        275                 280                 285

Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu His Asn Glu Gly Ala
    290                 295                 300

Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp Ile Phe Arg Thr Leu
305                 310                 315                 320

Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly Phe Asp Phe Met Pro
                325                 330                 335

Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys Lys Arg Val Gly Asp
            340                 345                 350

Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu Glu Leu Gly Ile Leu
        355                 360                 365

Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln Ile Phe Thr Lys Pro
    370                 375                 380

Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile Ile Gln Arg Val Gly
385                 390                 395                 400

Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr Gln Ser Gly Gly Cys
                405                 410                 415

Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu Phe Lys Ser Ile Glu
```

```
            420                 425                 430

Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu Val Gly
        435                 440                 445


<210>  3
<211>  1341
<212>  DNA
<213>  Oryza sativa

<400>  3
atgcctccca ctcccacccc caccgccacc accggcgccg tctcggccgc tgcggcggcg      60

ggggagaacg cggggttccg cctcgtcggg caccgccgct tcgtccgcgc caacccgcgg     120

agcgaccggt tccaggcgct cgcgttccac cacgtcgagc tctggtgcgc cgacgccgcg     180

tccgccgcgg gccggttcgc cttcgccctg ggcgcgccgc tcgccgccag gtccgacctc     240

tccacgggga actccgcgca cgcctccctc ctcctccgct ccgcctccgt cgcgttcctc     300

ttcaccgccc cctacggcgg cgaccacggc gtcggcgcgg acgcggccac caccgcctcc     360

atcccttcct tctccccagg cgccgcgcgg aggttcgccg cggaccacgg cctcgcggtg     420

cacgccgtgg cgctgcgcgt cgccgacgcg gccgacgcct tccgcgccag cgtcgcggcc     480

ggtgcgcgcc cggcgttcca gcccgccgac ctcggcggtg gcttcggcct cgcggaggtg     540

gagctctacg gcgacgtcgt gctccgcttc gtcagccacc cggacggcgc cgacgcgccc     600

ttcctcccgg gtttcgaggg cgtcagcaac ccgggcgccg tggactacgg cctccgccgg     660

ttcgaccacg tcgtcggcaa cgtgccggag ctcgctccgg tagccgcgta catctccggg     720

ttcaccgggt tccacgagtt cgccgagttc accgccgagg acgtgggcac cgccgagagc     780

ggcctcaact cggtggtgct cgccaacaac gcggagaccg tgctgctgcc gctcaacgag     840

ccggtgcacg gcaccaagcg gcggagccag atacagacgt acctggacca ccacggcggc     900

ccgggggtgc agcacatcgc gctggccagc gacgacgtgc tcgggacgct gagggagatg     960

cgggcgcgct ccgccatggg cggcttcgag ttcttggcgc cgccgccgcc caactactac    1020

gacggcgtgc ggcggcgcgc cggggacgtg ctctcggagg agcagatcaa cgagtgccag    1080

gagctcgggg tgctcgtgga cagggatgac caggggggtgt tgctccagat cttcaccaag   1140

ccagtaggag acaggccaac ctttttcttg gagatgatac aaaggattgg gtgcatggag    1200

aaggatgaga gtgggcagga gtaccagaag ggcggctgcg gcgggtttgg gaagggcaac    1260

ttctcggagc tgttcaagtc cattgaggag tatgagaaat cccttgaagc caagcaagcc    1320

cctacagttc aaggatccta g                                              1341
```

```
<210>  4
<211>  446
<212>  PRT
<213>  Oryza sativa

<400>  4

Met Pro Pro Thr Pro Thr Pro Thr Ala Thr Thr Gly Ala Val Ser Ala
1               5                   10                  15

Ala Ala Ala Ala Gly Glu Asn Ala Gly Phe Arg Leu Val Gly His Arg
            20                  25                  30

Arg Phe Val Arg Ala Asn Pro Arg Ser Asp Arg Phe Gln Ala Leu Ala
        35                  40                  45

Phe His His Val Glu Leu Trp Cys Ala Asp Ala Ala Ser Ala Ala Gly
    50                  55                  60

Arg Phe Ala Phe Ala Leu Gly Ala Pro Leu Ala Ala Arg Ser Asp Leu
65                  70                  75                  80

Ser Thr Gly Asn Ser Ala His Ala Ser Leu Leu Leu Arg Ser Ala Ser
                85                  90                  95

Val Ala Phe Leu Phe Thr Ala Pro Tyr Gly Gly Asp His Gly Val Gly
            100                 105                 110

Ala Asp Ala Ala Thr Thr Ala Ser Ile Pro Ser Phe Ser Pro Gly Ala
        115                 120                 125

Ala Arg Arg Phe Ala Ala Asp His Gly Leu Ala Val His Ala Val Ala
    130                 135                 140

Leu Arg Val Ala Asp Ala Ala Asp Ala Phe Arg Ala Ser Val Ala Ala
145                 150                 155                 160

Gly Ala Arg Pro Ala Phe Gln Pro Ala Asp Leu Gly Gly Gly Phe Gly
                165                 170                 175

Leu Ala Glu Val Glu Leu Tyr Gly Asp Val Val Leu Arg Phe Val Ser
            180                 185                 190

His Pro Asp Gly Ala Asp Ala Pro Phe Leu Pro Gly Phe Glu Gly Val
        195                 200                 205
```

```
Ser Asn Pro Gly Ala Val Asp Tyr Gly Leu Arg Arg Phe Asp His Val
    210                 215                 220

Val Gly Asn Val Pro Glu Leu Ala Pro Val Ala Ala Tyr Ile Ser Gly
225                 230                 235                 240

Phe Thr Gly Phe His Glu Phe Ala Glu Phe Thr Ala Glu Asp Val Gly
                245                 250                 255

Thr Ala Glu Ser Gly Leu Asn Ser Val Val Leu Ala Asn Asn Ala Glu
            260                 265                 270

Thr Val Leu Leu Pro Leu Asn Glu Pro Val His Gly Thr Lys Arg Arg
        275                 280                 285

Ser Gln Ile Gln Thr Tyr Leu Asp His His Gly Gly Pro Gly Val Gln
    290                 295                 300

His Ile Ala Leu Ala Ser Asp Asp Val Leu Gly Thr Leu Arg Glu Met
305                 310                 315                 320

Arg Ala Arg Ser Ala Met Gly Gly Phe Glu Phe Leu Ala Pro Pro Pro
                325                 330                 335

Pro Asn Tyr Tyr Asp Gly Val Arg Arg Arg Ala Gly Asp Val Leu Ser
            340                 345                 350

Glu Glu Gln Ile Asn Glu Cys Gln Glu Leu Gly Val Leu Val Asp Arg
        355                 360                 365

Asp Asp Gln Gly Val Leu Leu Gln Ile Phe Thr Lys Pro Val Gly Asp
    370                 375                 380

Arg Pro Thr Phe Phe Leu Glu Met Ile Gln Arg Ile Gly Cys Met Glu
385                 390                 395                 400

Lys Asp Glu Ser Gly Gln Glu Tyr Gln Lys Gly Gly Cys Gly Gly Phe
                405                 410                 415

Gly Lys Gly Asn Phe Ser Glu Leu Phe Lys Ser Ile Glu Glu Tyr Glu
            420                 425                 430

Lys Ser Leu Glu Ala Lys Gln Ala Pro Thr Val Gln Gly Ser
        435                 440                 445
```

<210> 5
<211> 1281
<212> DNA
<213> Zea mays

<400> 5
atgcccccga cccccacagc cgccgcagcc ggcgccgccg tggcggcggc atcagcagcg 60

gagcaggcgg cgttccgcct cgtgggccac cgcaacttcg tccgcttcaa cccgcgctcc 120

gaccgcttcc acacgctcgc gttccaccac gtggagctct ggtgcgccga cgcggcctcc 180

gccgcgggcc gcttctcctt cggcctgggc gcgccgctcg ccgcacgctc cgacctctcc 240

acgggcaact ccgcgcacgc gtccctgctg ctccgctccg gctccctctc cttcctcttc 300

acggcgccct acgcgcacgg cgccgacgct gccaccgccg cgctgccctc cttctccgcc 360

gccgccgcgc ggcgcttcgc agccgaccac ggcctcgcgg tgcgcgccgt cgcgctccgc 420

gtcgccgacg ccgaggacgc cttccgcggc ttccgcctcg ccgaggtcga gctctacggc 480

gacgtcgtgc tccggtacgt gagctacccg gacggcgccg cgggcgagcc cttcctgccg 540

gggttcgagg gcgtggccag ccccggggcg gccgactacg ggctgagcag gttcgaccac 600

atcgtcggca acgtgccgga gctggcgccc gccgccgcct acttcgccgg cttcacgggg 660

ttccacgagt tcgccgagtt cacgacggag gacgtgggca ccgcggagag cggcctcaac 720

tccatggtgc tcgccaacaa ctcggagaac gtgctgctcc cgctcaacga gccggtgcac 780

ggcaccaagc gccgcagcca gatacaaacg ttcctggacc accacggcgg ccccggcgtg 840

cagcacatgg cgctggccag cgacgacgtg ctcaggacgc tgagggagat gcaggcgcgc 900

tcggccatgg gcggcttcga gttcatggcg cctcccacat ccgactacta tgacggcgtg 960

aggcggcgcg ccggggacgt gctcacggaa gcacagatta aggagtgcca ggagctaggg 1020

gtgctggtgg acagggatga ccagggcgtg ctgctccaaa tcttcaccaa gccagtgggg 1080

gacaggccaa cgctgttctt ggaaatcatc caaaggatcg ggtgcatgga gaaggatgag 1140

aaggggcaag aataccaaaa gggtggctgc ggcgggttcg gcaagggaaa cttctcgcag 1200

ctgttcaagt ccatcgagga ttatgagaag tcccttgaag ccaagcaagc tgctgcagca 1260

gctgcagctc agggatccta g 1281

<210> 6
<211> 426
<212> PRT
<213> Zea mays

<400> 6

```
Met Pro Pro Thr Pro Thr Ala Ala Ala Ala Gly Ala Ala Val Ala Ala
1               5                   10                  15

Ala Ser Ala Ala Glu Gln Ala Ala Phe Arg Leu Val Gly His Arg Asn
            20                  25                  30

Phe Val Arg Phe Asn Pro Arg Ser Asp Arg Phe His Thr Leu Ala Phe
        35                  40                  45

His His Val Glu Leu Trp Cys Ala Asp Ala Ala Ser Ala Ala Gly Arg
    50                  55                  60

Phe Ser Phe Gly Leu Gly Ala Pro Leu Ala Ala Arg Ser Asp Leu Ser
65                  70                  75                  80

Thr Gly Asn Ser Ala His Ala Ser Leu Leu Leu Arg Ser Gly Ser Leu
                85                  90                  95

Ser Phe Leu Phe Thr Ala Pro Tyr Ala His Gly Ala Asp Ala Ala Thr
            100                 105                 110

Ala Ala Leu Pro Ser Phe Ser Ala Ala Ala Ala Arg Arg Phe Ala Ala
        115                 120                 125

Asp His Gly Leu Ala Val Arg Ala Val Ala Leu Arg Val Ala Asp Ala
    130                 135                 140

Glu Asp Ala Phe Arg Gly Phe Arg Leu Ala Glu Val Glu Leu Tyr Gly
145                 150                 155                 160

Asp Val Val Leu Arg Tyr Val Ser Tyr Pro Asp Gly Ala Ala Gly Glu
                165                 170                 175

Pro Phe Leu Pro Gly Phe Glu Gly Val Ala Ser Pro Gly Ala Ala Asp
            180                 185                 190

Tyr Gly Leu Ser Arg Phe Asp His Ile Val Gly Asn Val Pro Glu Leu
        195                 200                 205

Ala Pro Ala Ala Ala Tyr Phe Ala Gly Phe Thr Gly Phe His Glu Phe
    210                 215                 220

Ala Glu Phe Thr Thr Glu Asp Val Gly Thr Ala Glu Ser Gly Leu Asn
225                 230                 235                 240
```

```
Ser Met Val Leu Ala Asn Asn Ser Glu Asn Val Leu Leu Pro Leu Asn
                245                 250                 255

Glu Pro Val His Gly Thr Lys Arg Arg Ser Gln Ile Gln Thr Phe Leu
            260                 265                 270

Asp His His Gly Gly Pro Gly Val Gln His Met Ala Leu Ala Ser Asp
        275                 280                 285

Asp Val Leu Arg Thr Leu Arg Glu Met Gln Ala Arg Ser Ala Met Gly
    290                 295                 300

Gly Phe Glu Phe Met Ala Pro Pro Thr Ser Asp Tyr Tyr Asp Gly Val
305                 310                 315                 320

Arg Arg Arg Ala Gly Asp Val Leu Thr Glu Ala Gln Ile Lys Glu Cys
                325                 330                 335

Gln Glu Leu Gly Val Leu Val Asp Arg Asp Asp Gln Gly Val Leu Leu
            340                 345                 350

Gln Ile Phe Thr Lys Pro Val Gly Asp Arg Pro Thr Leu Phe Leu Glu
        355                 360                 365

Ile Ile Gln Arg Ile Gly Cys Met Glu Lys Asp Glu Lys Gly Gln Glu
    370                 375                 380

Tyr Gln Lys Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Gln
385                 390                 395                 400

Leu Phe Lys Ser Ile Glu Asp Tyr Glu Lys Ser Leu Glu Ala Lys Gln
                405                 410                 415

Ala Ala Ala Ala Ala Ala Ala Gln Gly Ser
            420                 425


<210>  7
<211>  1323
<212>  DNA
<213>  Avena sativa

<400>  7
atgccgccca cccccgccac cgccaccggc gccgccgcgg ccgccgtgac tccagagcac      60

gcggcccgga gctttccccg agtggtccgc gtcaacccgc gcagcgaccg cttccccgtg     120
```

```
ctctccttcc accacgtcga gctctggtgc gccgacgccg cctcagcggc cggacgcttc    180

tccttcgcgc tcggcgcgcc gctcgccgcc cggtccgacc tctccacggg gaactccgcg    240

cacgcctccc tcctgctccg ctcgggcgcc ctcgccttcc tcttcacggc gccctacgcg    300

ccgccgccgc aggaggccgc cacggccgca gccaccgcct ccatcccctc cttctccgcc    360

gacgccgcgc ggacgttcgc cgccgcccac ggcctcgcgg tgcgctccgt cggggtccgc    420

gtcgctgacg ccgccgaggc cttccgcgtc agcgtagccg gcggcgctcg cccggccttc    480

gccccagccg acctcggcca tggcttcggc ctcgccgagg tcgagctcta cggcgacgtc    540

gtgctacgct tcgtcagcta cccggacgag acagacctgc cattcctgcc agggttcgag    600

cgcgtgagca gccccggcgc cgtggactac ggcctcacgc ggttcgacca cgtcgtgggc    660

aacgtcccgg agatggcccc ggtcatagac tacatgaaag gcttcttggg gttccacgag    720

ttcgccgagt tcaccgccga ggacgtgggc acgaccgaga gcgggctcaa ctcggtggtg    780

ctcgccaaca actccgaggc cgtgctgctg ccgctcaacg agcccgtgca cggcacaaag    840

cgacggagcc agatacagac gtacctggag tatcacggcg ggcccggcgt gcagcacatc    900

gcgctcgcca gcaacgacgt gctcaggacg ctcagggaga tgcgggcgcg cacgcccatg    960

ggcggcttcg agttcatggc gccaccgcag gcgaaatact atgaaggcgt gcggcgcatc   1020

gcaggtgacg tgctctcgga agagcagatc aaggaatgcc aggagctggg ggtgctagtc   1080

gacagggatg atcaaggggt gttgctccaa atcttcacca agccagtagg ggacaggcca   1140

acgtttttcc tggagatgat ccaaagaatc gggtgcatgg agaaggacga ggtcgggcaa   1200

gagtaccaga agggtggctg cggcgggttt ggcaagggca atttctccga gctgttcaag   1260

tccattgagg actatgagaa atcccttgag gtcaagcaat ctgttgtagc tcagaaatcc   1320

tag                                                                 1323


<210>  8
<211>  440
<212>  PRT
<213>  Avena sativa

<400>  8

Met Pro Pro Thr Pro Ala Thr Ala Thr Gly Ala Ala Ala Ala Ala Val
1               5                   10                  15


Thr Pro Glu His Ala Ala Arg Ser Phe Pro Arg Val Val Arg Val Asn
            20                  25                  30
```

```
Pro Arg Ser Asp Arg Phe Pro Val Leu Ser Phe His His Val Glu Leu
        35                  40                  45

Trp Cys Ala Asp Ala Ala Ser Ala Ala Gly Arg Phe Ser Phe Ala Leu
    50                  55                  60

Gly Ala Pro Leu Ala Ala Arg Ser Asp Leu Ser Thr Gly Asn Ser Ala
65                  70                  75                  80

His Ala Ser Leu Leu Leu Arg Ser Gly Ala Leu Ala Phe Leu Phe Thr
                85                  90                  95

Ala Pro Tyr Ala Pro Pro Pro Gln Glu Ala Ala Thr Ala Ala Ala Thr
            100                 105                 110

Ala Ser Ile Pro Ser Phe Ser Ala Asp Ala Ala Arg Thr Phe Ala Ala
        115                 120                 125

Ala His Gly Leu Ala Val Arg Ser Val Gly Val Arg Val Ala Asp Ala
    130                 135                 140

Ala Glu Ala Phe Arg Val Ser Val Ala Gly Gly Ala Arg Pro Ala Phe
145                 150                 155                 160

Ala Pro Ala Asp Leu Gly His Gly Phe Gly Leu Ala Glu Val Glu Leu
                165                 170                 175

Tyr Gly Asp Val Val Leu Arg Phe Val Ser Tyr Pro Asp Glu Thr Asp
            180                 185                 190

Leu Pro Phe Leu Pro Gly Phe Glu Arg Val Ser Ser Pro Gly Ala Val
        195                 200                 205

Asp Tyr Gly Leu Thr Arg Phe Asp His Val Val Gly Asn Val Pro Glu
    210                 215                 220

Met Ala Pro Val Ile Asp Tyr Met Lys Gly Phe Leu Gly Phe His Glu
225                 230                 235                 240

Phe Ala Glu Phe Thr Ala Glu Asp Val Gly Thr Thr Glu Ser Gly Leu
                245                 250                 255

Asn Ser Val Val Leu Ala Asn Asn Ser Glu Ala Val Leu Leu Pro Leu
            260                 265                 270
```

```
Asn Glu Pro Val His Gly Thr Lys Arg Arg Ser Gln Ile Gln Thr Tyr
        275                 280                 285

Leu Glu Tyr His Gly Gly Pro Gly Val Gln His Ile Ala Leu Ala Ser
    290                 295                 300

Asn Asp Val Leu Arg Thr Leu Arg Glu Met Arg Ala Arg Thr Pro Met
305                 310                 315                 320

Gly Gly Phe Glu Phe Met Ala Pro Pro Gln Ala Lys Tyr Tyr Glu Gly
                325                 330                 335

Val Arg Arg Ile Ala Gly Asp Val Leu Ser Glu Glu Gln Ile Lys Glu
            340                 345                 350

Cys Gln Glu Leu Gly Val Leu Val Asp Arg Asp Asp Gln Gly Val Leu
        355                 360                 365

Leu Gln Ile Phe Thr Lys Pro Val Gly Asp Arg Pro Thr Phe Phe Leu
    370                 375                 380

Glu Met Ile Gln Arg Ile Gly Cys Met Glu Lys Asp Glu Val Gly Gln
385                 390                 395                 400

Glu Tyr Gln Lys Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser
                405                 410                 415

Glu Leu Phe Lys Ser Ile Glu Asp Tyr Glu Lys Ser Leu Glu Val Lys
            420                 425                 430

Gln Ser Val Val Ala Gln Lys Ser
        435                 440


<210>  9
<211>  1077
<212>  DNA
<213>  Pseudomonas fluorescens

<400>  9
atggcagatc tatacgaaaa cccaatgggc ctgatgggct ttgaattcat cgaattcgcg      60

tcgccgacgc cgggtaccct ggagccgatc ttcgagatca tgggcttcac caaagtcgcg     120

acccaccgtt ccaagaacgt gcacctgtac cgccagggcg agatcaacct gatcctcaac     180

aacgagccca acagcatcgc ctcctacttt gcggccgaac acggcccgtc ggtgtgcggc     240
```

```
atggcgttcc gcgtgaagga ctcgcaaaag gcctacaacc gcgccctgga actcggcgcc     300

cagccgatcc atattgacac cgggccgatg gaattgaacc tgccggcgat caagggcatc     360

ggcggcgcgc cgttgtacct gatcgaccgt ttcggcgaag gcagctcgat ctacgacatc     420

gacttcgtgt acctcgaagg tgtggagcgc aatccggtcg gtgcaggtct caaagtcatc     480

gaccacctga cccacaacgt ctatcgcggc cgcatggtct actgggccaa cttctacgag     540

aaattgttca acttccgtga agcgcgttac ttcgatatca agggcgagta caccggcctg     600

acttccaagg ccatgagtgc gccggacggc atgatccgca tcccgctgaa cgaagagtcg     660

tccaagggcg cggggcagat cgaagagttc ctgatgcagt tcaacggcga aggcatccag     720

cacgtggcgt tcctcaccga cgacctggtc aagacctggg acgcgttgaa gaaaatcggc     780

atgcgcttca tgaccgcgcc gccagacact tattacgaaa tgctcgaagg ccgcctgcct     840

gaccacggcg agccggtgga tcaactgcag gcacgcggta tcctgctgga cggatcttcc     900

gtggaaggcg acaaacgcct gctgctgcag atcttctcgg aaaccctgat gggcccggtg     960

ttcttcgaat tcatccagcg caagggcgac gatgggtttg gcgagggcaa cttcaaggcg    1020

ctgttcgagt ccatcgaacg tgaccaggtg cgtcgtggtg tattgaccgc cgattaa       1077


<210>  10
<211>  358
<212>  PRT
<213>  Pseudomonas fluorescens

<400>  10

Met Ala Asp Leu Tyr Glu Asn Pro Met Gly Leu Met Gly Phe Glu Phe
1               5                   10                  15


Ile Glu Phe Ala Ser Pro Thr Pro Gly Thr Leu Glu Pro Ile Phe Glu
            20                  25                  30


Ile Met Gly Phe Thr Lys Val Ala Thr His Arg Ser Lys Asn Val His
        35                  40                  45


Leu Tyr Arg Gln Gly Glu Ile Asn Leu Ile Leu Asn Asn Glu Pro Asn
    50                  55                  60


Ser Ile Ala Ser Tyr Phe Ala Ala Glu His Gly Pro Ser Val Cys Gly
65                  70                  75                  80


Met Ala Phe Arg Val Lys Asp Ser Gln Lys Ala Tyr Asn Arg Ala Leu
                85                  90                  95
```

```
Glu Leu Gly Ala Gln Pro Ile His Ile Asp Thr Gly Pro Met Glu Leu
            100                 105                 110

Asn Leu Pro Ala Ile Lys Gly Ile Gly Gly Ala Pro Leu Tyr Leu Ile
        115                 120                 125

Asp Arg Phe Gly Glu Gly Ser Ser Ile Tyr Asp Ile Asp Phe Val Tyr
    130                 135                 140

Leu Glu Gly Val Glu Arg Asn Pro Val Gly Ala Gly Leu Lys Val Ile
145                 150                 155                 160

Asp His Leu Thr His Asn Val Tyr Arg Gly Arg Met Val Tyr Trp Ala
                165                 170                 175

Asn Phe Tyr Glu Lys Leu Phe Asn Phe Arg Glu Ala Arg Tyr Phe Asp
            180                 185                 190

Ile Lys Gly Glu Tyr Thr Gly Leu Thr Ser Lys Ala Met Ser Ala Pro
        195                 200                 205

Asp Gly Met Ile Arg Ile Pro Leu Asn Glu Glu Ser Ser Lys Gly Ala
    210                 215                 220

Gly Gln Ile Glu Glu Phe Leu Met Gln Phe Asn Gly Glu Gly Ile Gln
225                 230                 235                 240

His Val Ala Phe Leu Thr Asp Asp Leu Val Lys Thr Trp Asp Ala Leu
                245                 250                 255

Lys Lys Ile Gly Met Arg Phe Met Thr Ala Pro Pro Asp Thr Tyr Tyr
            260                 265                 270

Glu Met Leu Glu Gly Arg Leu Pro Asp His Gly Glu Pro Val Asp Gln
        275                 280                 285

Leu Gln Ala Arg Gly Ile Leu Leu Asp Gly Ser Ser Val Glu Gly Asp
    290                 295                 300

Lys Arg Leu Leu Leu Gln Ile Phe Ser Glu Thr Leu Met Gly Pro Val
305                 310                 315                 320

Phe Phe Glu Phe Ile Gln Arg Lys Gly Asp Asp Gly Phe Gly Glu Gly
                325                 330                 335
```

```
Asn Phe Lys Ala Leu Phe Glu Ser Ile Glu Arg Asp Gln Val Arg Arg
            340                 345                 350

Gly Val Leu Thr Ala Asp
        355


<210>  13
<211>  1053
<212>  DNA
<213>  Synechococcus sp.

<400>  13
atgaacccgt ccattcgaat tgtccaaggg atccaccacc tgcacttcta cctttgggat      60

ctgccccgtt ggcgggaaca cttttgtcgg gtttggggct tccgggtggc aagcgacgcc     120

ggcaacaccc tggagctgga gcagggatcc ctgcgcttgc gcctgtctca gccggcacgg     180

gcgggggacg aggtggaccg ccatttgcag cggcatgggc cgggggtggt ggatgtggcc     240

ttggcggtgg gagagcagga gctaccggcc ttggcggagc tgttgcgggg ccgaggcgcc     300

caactggcgt ggatcccggc agcagcggcg ctctgcctcc acacccccta cgggatccgg     360

cattctctga tccctggccc cttggatgcc gcccctgccg aagcgggcct gttttcccac     420

tgggatcacg tggtgttgaa cgtggagcag ggatccctgc aggcggcagc cgactggtat     480

gggcgggtgc tgggctggcg gcggctgtac cgctacagca tcggcaccgc cacctccggc     540

ctggaaagcg tggtggtggg ggatccggaa gcggggatcc aatgggccat caacgagccc     600

acctgtgccg cttcccagat tcaggagttt ttgcatgccc atggcggccc gggcattcag     660

cacgcggcgc tgcacagctc agacattgtt gccagcctgc gccggttgcg gcaggggga      720

gtggactttt tgcaagtggc gccgcagtac tacaccagcc tggaaaggga gctggggttg     780

gcgctccgtt ctgcccttgg gcaggccatc tcctggcaag acctggtgga gcagcagatc     840

cttctggatg ctaccctgcc cgcttctgat ggccaggatc gccccccttct gctgcagacc     900

tttacccagc cctctttgg tcggcccacc tttttctttg aagtcattca acggctaggc      960

ggggccacgg gctttggcga ggccaatttt caggctttgt tcgaggccct ggaacggcaa    1020

cagcgacagc gacaccaggc gctgacccct tag                                 1053


<210>  14
<211>  350
<212>  PRT
<213>  Synechococcus sp.

<400>  14
```

```
Met Asn Pro Ser Ile Arg Ile Val Gln Gly Ile His His Leu His Phe
1               5                   10                  15

Tyr Leu Trp Asp Leu Pro Arg Trp Arg Glu His Phe Cys Arg Val Trp
            20                  25                  30

Gly Phe Arg Val Ala Ser Asp Ala Gly Asn Thr Leu Glu Leu Glu Gln
        35                  40                  45

Gly Ser Leu Arg Leu Arg Leu Ser Gln Pro Ala Arg Ala Gly Asp Glu
    50                  55                  60

Val Asp Arg His Leu Gln Arg His Gly Pro Gly Val Val Asp Val Ala
65                  70                  75                  80

Leu Ala Val Gly Glu Gln Glu Leu Pro Ala Leu Ala Glu Leu Leu Arg
                85                  90                  95

Gly Arg Gly Ala Gln Leu Ala Trp Ile Pro Ala Ala Ala Ala Leu Cys
            100                 105                 110

Leu His Thr Pro Tyr Gly Ile Arg His Ser Leu Ile Pro Gly Pro Leu
        115                 120                 125

Asp Ala Ala Pro Ala Glu Ala Gly Leu Phe Ser His Trp Asp His Val
    130                 135                 140

Val Leu Asn Val Glu Gln Gly Ser Leu Gln Ala Ala Ala Asp Trp Tyr
145                 150                 155                 160

Gly Arg Val Leu Gly Trp Arg Arg Leu Tyr Arg Tyr Ser Ile Gly Thr
                165                 170                 175

Ala Thr Ser Gly Leu Glu Ser Val Val Val Gly Asp Pro Glu Ala Gly
            180                 185                 190

Ile Gln Trp Ala Ile Asn Glu Pro Thr Cys Ala Ala Ser Gln Ile Gln
        195                 200                 205

Glu Phe Leu His Ala His Gly Gly Pro Gly Ile Gln His Ala Ala Leu
    210                 215                 220

His Ser Ser Asp Ile Val Ala Ser Leu Arg Arg Leu Arg Gln Gly Gly
225                 230                 235                 240
```

```
Val Asp Phe Leu Gln Val Ala Pro Gln Tyr Tyr Thr Ser Leu Glu Arg
                245                 250                 255

Glu Leu Gly Leu Ala Leu Arg Ser Ala Leu Gly Gln Ala Ile Ser Trp
            260                 265                 270

Gln Asp Leu Val Glu Gln Gln Ile Leu Leu Asp Ala Thr Leu Pro Ala
        275                 280                 285

Ser Asp Gly Gln Asp Arg Pro Leu Leu Leu Gln Thr Phe Thr Gln Pro
    290                 295                 300

Leu Phe Gly Arg Pro Thr Phe Phe Phe Glu Val Ile Gln Arg Leu Gly
305                 310                 315                 320

Gly Ala Thr Gly Phe Gly Glu Ala Asn Phe Gln Ala Leu Phe Glu Ala
                325                 330                 335

Leu Glu Arg Gln Gln Arg Gln Arg His Gln Ala Leu Thr Pro
            340                 345                 350


<210>  15
<211>  1149
<212>  DNA
<213>  Blepharisma japonicum

<400>  15
atgacttatt acgacaagca agaaacgcgt ccagatcttg gcgaattcta tggtttccat      60

cacgttcgtt tttacgtctc caactcagag caagccgctt cgttctacac atctcgcttt     120

gggttttctc cggttgccta tgaaggattg gaaacaggaa accaaaaatt ctgtaccaat     180

gtcgtccgaa gcaaccatgt agtcatcgct tttacctcag ctctcactcc tgaagacaat     240

gaagtgaacc gtcacgttgg caagcatagt gatggagttc aagacattgc ctttagtgta     300

agtgacgcaa gagggatgta tgagaaagcg atagctaaag gctgtaaaag cttccgtgag     360

ccacaggttt tacaagatca atttggatct gttataatag cgtctctcca gacttatgga     420

gacactgttc acacattagt ccaaaatgtc gactatacag gacccttttt gcctggcttc     480

agagcaatca caaaagatga tccattaaac tctgcctttc ctcaggtaaa ttatgacatt     540

attgatcatg ttgtaggaaa tcagcctggt ggcgatatga ctcctacagt agaatggtat     600

gagaaatatc tagaatttca tcgatattgg tctgctgatg agtctgtaat ccataccgat     660

tattcagcat taaggtctgt tgtggttgct gattgggatg aagtgatcaa aatgcctatt     720
```

```
aatgagcctg ctgatggact tagaaaaagt caaatccaag aatatgtcga atattatggt     780

ggagcaggcg tacaacatat tgccttaaaa gtcaatgata ttatttcagt aataagcacc     840

ttaagggcta gaggtgtgga attcttagaa gttcctccta aatattatga tagcttaaga     900

aaaagacttg cgcattctgc ggtacaaatt gaagaagact taaaaagaat tgaagacctt     960

catattttgg ttgactttga cgaccgtggg tatttacttc agattttcac aaaaccagta    1020

gaagacagac ctactctgtt ttatgaaatt attcaaagac ataataacaa tggattcgga    1080

attggaaatt ttaaagccct atttgaatca ttggaacaag agcaagaaag aagaggtaat    1140

ttgatctaa                                                            1149


<210>  16
<211>  382
<212>  PRT
<213>  Blepharisma japonicum

<400>  16

Met Thr Tyr Tyr Asp Lys Gln Glu Thr Arg Pro Asp Leu Gly Glu Phe
1               5                   10                  15


Tyr Gly Phe His His Val Arg Phe Tyr Val Ser Asn Ser Glu Gln Ala
            20                  25                  30


Ala Ser Phe Tyr Thr Ser Arg Phe Gly Phe Ser Pro Val Ala Tyr Glu
        35                  40                  45


Gly Leu Glu Thr Gly Asn Gln Lys Phe Cys Thr Asn Val Val Arg Ser
    50                  55                  60


Asn His Val Val Ile Ala Phe Thr Ser Ala Leu Thr Pro Glu Asp Asn
65                  70                  75                  80


Glu Val Asn Arg His Val Gly Lys His Ser Asp Gly Val Gln Asp Ile
                85                  90                  95


Ala Phe Ser Val Ser Asp Ala Arg Gly Met Tyr Glu Lys Ala Ile Ala
            100                 105                 110


Lys Gly Cys Lys Ser Phe Arg Glu Pro Gln Val Leu Gln Asp Gln Phe
        115                 120                 125


Gly Ser Val Ile Ile Ala Ser Leu Gln Thr Tyr Gly Asp Thr Val His
    130                 135                 140
```

```
Thr Leu Val Gln Asn Val Asp Tyr Thr Gly Pro Phe Leu Pro Gly Phe
145                 150                 155                 160

Arg Ala Ile Thr Lys Asp Asp Pro Leu Asn Ser Ala Phe Pro Gln Val
                165                 170                 175

Asn Tyr Asp Ile Ile Asp His Val Val Gly Asn Gln Pro Gly Gly Asp
            180                 185                 190

Met Thr Pro Thr Val Glu Trp Tyr Glu Lys Tyr Leu Glu Phe His Arg
        195                 200                 205

Tyr Trp Ser Ala Asp Glu Ser Val Ile His Thr Asp Tyr Ser Ala Leu
    210                 215                 220

Arg Ser Val Val Val Ala Asp Trp Asp Glu Val Ile Lys Met Pro Ile
225                 230                 235                 240

Asn Glu Pro Ala Asp Gly Leu Arg Lys Ser Gln Ile Gln Glu Tyr Val
                245                 250                 255

Glu Tyr Tyr Gly Gly Ala Gly Val Gln His Ile Ala Leu Lys Val Asn
            260                 265                 270

Asp Ile Ile Ser Val Ile Ser Thr Leu Arg Ala Arg Gly Val Glu Phe
        275                 280                 285

Leu Glu Val Pro Pro Lys Tyr Tyr Asp Ser Leu Arg Lys Arg Leu Ala
    290                 295                 300

His Ser Ala Val Gln Ile Glu Glu Asp Leu Lys Arg Ile Glu Asp Leu
305                 310                 315                 320

His Ile Leu Val Asp Phe Asp Asp Arg Gly Tyr Leu Leu Gln Ile Phe
                325                 330                 335

Thr Lys Pro Val Glu Asp Arg Pro Thr Leu Phe Tyr Glu Ile Ile Gln
            340                 345                 350

Arg His Asn Asn Asn Gly Phe Gly Ile Gly Asn Phe Lys Ala Leu Phe
        355                 360                 365

Glu Ser Leu Glu Gln Glu Gln Glu Arg Arg Gly Asn Leu Ile
```

```
    370                 375                 380


<210>  17
<211>  1206
<212>  DNA
<213>  Rhodococcus sp.

<400>  17
atgacgatcg agcagactct caccgacaag gaacgcctgg caggtctcga cctcggccag      60

ctcgagcagt tggtcgggct cgtcgagtac gacggcaccc gcgacccgtt cccggtcagc     120

ggctgggatg ccgtcgtctg ggtggtcggc aacgccaccc agaccgccca ctacttccag     180

tccgcgttcg ggatgaccct cgtcgcctac tccggaccca ccaccggcaa ccgcgaccac     240

cacagcttcg tcctcgaatc cggggccgtc cgcttcgtca tcaaaggcgc cgtgaacccg     300

gacagccccc tgatcgacca ccaccgcacc cacggcgacg gcgtcgtcga catcgccctc     360

gccgtccccg acgtcgacaa gtgcatcgcc cacgcccgcg cccagggcgc caccgtcctc     420

gacgaacccc acgacgtgac cgacgaccac ggcaccgtcc gcctcgccgc gatcgccacc     480

tacggcgaca cccgccacac cctcgtcgac cgcagccact acaccggccc ctacctgccc     540

ggctacaccg cccgcacctc cggccacacc aaacgggacg ggcacccaa gcgcctgttc      600

caggccctcg accacgtcgt cggcaacgtc gaactcggca agatggacca ctgggtcgac     660

ttctacaacc gggtcatggg ctttacgaac atggccgagt tcgtcggcga ggacatcgcc     720

accgactact ccgcgctgat gagcaaggtc gtctccaacg gcaaccaccg ggtcaagttc     780

cccctcaacg aacccgccct cgccaagaaa cgctcgcaga tcgacgaata cctcgacttc     840

taccgcggcc ccggcgccca gcacctggcc ctggccacca atgacatcct caccgccgtc     900

gaccagctga ccgccgaggg cgtcgagttc ctggccaccc ccgactccta ctacgaggac     960

cccgaactgc gggcccggat cggcaacgtc cgcgccccca tcgccgaact gcagaaacgc    1020

ggcatcctcg tcgaccgcga cgaagacggc tacctgctgc agatcttcac caaacccctc    1080

gtcgaccggc ccaccgtgtt cttcgaactc atcgaacgcc acggctccct cggcttcggc    1140

atcggcaact tcaaagccct cttcgaggcc atcgaacgcg aacaagccgc ccgcggaaac    1200

ttctga                                                               1206


<210>  18
<211>  401
<212>  PRT
<213>  Rhodococcus sp.

<400>  18
```

```
Met Thr Ile Glu Gln Thr Leu Thr Asp Lys Glu Arg Leu Ala Gly Leu
1               5                   10                  15

Asp Leu Gly Gln Leu Glu Gln Leu Val Gly Leu Val Glu Tyr Asp Gly
            20                  25                  30

Thr Arg Asp Pro Phe Pro Val Ser Gly Trp Asp Ala Val Val Trp Val
        35                  40                  45

Val Gly Asn Ala Thr Gln Thr Ala His Tyr Phe Gln Ser Ala Phe Gly
    50                  55                  60

Met Thr Leu Val Ala Tyr Ser Gly Pro Thr Thr Gly Asn Arg Asp His
65                  70                  75                  80

His Ser Phe Val Leu Glu Ser Gly Ala Val Arg Phe Val Ile Lys Gly
                85                  90                  95

Ala Val Asn Pro Asp Ser Pro Leu Ile Asp His His Arg Thr His Gly
            100                 105                 110

Asp Gly Val Val Asp Ile Ala Leu Ala Val Pro Asp Val Asp Lys Cys
        115                 120                 125

Ile Ala His Ala Arg Ala Gln Gly Ala Thr Val Leu Asp Glu Pro His
    130                 135                 140

Asp Val Thr Asp Asp His Gly Thr Val Arg Leu Ala Ala Ile Ala Thr
145                 150                 155                 160

Tyr Gly Asp Thr Arg His Thr Leu Val Asp Arg Ser His Tyr Thr Gly
                165                 170                 175

Pro Tyr Leu Pro Gly Tyr Thr Ala Arg Thr Ser Gly His Thr Lys Arg
            180                 185                 190

Asp Gly Ala Pro Lys Arg Leu Phe Gln Ala Leu Asp His Val Val Gly
        195                 200                 205

Asn Val Glu Leu Gly Lys Met Asp His Trp Val Asp Phe Tyr Asn Arg
    210                 215                 220

Val Met Gly Phe Thr Asn Met Ala Glu Phe Val Gly Glu Asp Ile Ala
225                 230                 235                 240
```

```
Thr Asp Tyr Ser Ala Leu Met Ser Lys Val Val Ser Asn Gly Asn His
                245                 250                 255

Arg Val Lys Phe Pro Leu Asn Glu Pro Ala Leu Ala Lys Lys Arg Ser
            260                 265                 270

Gln Ile Asp Glu Tyr Leu Asp Phe Tyr Arg Gly Pro Gly Ala Gln His
        275                 280                 285

Leu Ala Leu Ala Thr Asn Asp Ile Leu Thr Ala Val Asp Gln Leu Thr
    290                 295                 300

Ala Glu Gly Val Glu Phe Leu Ala Thr Pro Asp Ser Tyr Tyr Glu Asp
305                 310                 315                 320

Pro Glu Leu Arg Ala Arg Ile Gly Asn Val Arg Ala Pro Ile Ala Glu
                325                 330                 335

Leu Gln Lys Arg Gly Ile Leu Val Asp Arg Asp Glu Asp Gly Tyr Leu
            340                 345                 350

Leu Gln Ile Phe Thr Lys Pro Leu Val Asp Arg Pro Thr Val Phe Phe
        355                 360                 365

Glu Leu Ile Glu Arg His Gly Ser Leu Gly Phe Gly Ile Gly Asn Phe
    370                 375                 380

Lys Ala Leu Phe Glu Ala Ile Glu Arg Glu Gln Ala Ala Arg Gly Asn
385                 390                 395                 400

Phe


<210>  19
<211>  1107
<212>  DNA
<213>  Picrophilus torridus

<400>  19
atgtatggca aaaatttaat ctcagaacta agggaaaagg agatctttaa acgattacat      60

cacgtggaat tttacgttag cagtgccaaa acatggtcat atttcatgaa caggggtctt     120

ggatttaaaa cagtggcata tgccggtcca gaaaccggga taagggacaa gatatcctat     180

gttatgtccc agggcactgc aaggatatct tttacatcat caatgaatga tgatagctat     240
```

```
atatcgaatc atgttaaaaa acacggggat ggcgtaaagg atatagcact tgaggtcgat    300

gatctggacg aggcaaaaag cctgatagaa aagtatggaa caaaggtttc aaaaataaat    360

gaaataaagg atggaaatgg aaagataaga actgcagaga taaaaacgta cggtgaaacc    420

gttcatacat taatagaaac cggggattac aatggcgtat tcatgcccgg ttatgaggaa    480

tctgaaataa attcaaaaaa cactgggata aaaaagatcg atcatatagt tggaaatgtc    540

tatgagggcg agatggatag ctgggttaat ttttacatag aaaaacttgg ctttgagcat    600

ttaataacct ttgatgataa agatataaga actgattaca gcgcattaag atcaaaggtt    660

gtaaaataca atgacgatat cgtatttcca ataaatgagc ctgcaaaggg cttaagaaaa    720

tcacagatag aggaatatct tgactattac aggtctgagg gcgttcagca catagcactg    780

ttaactgatg atataataaa aactgtatcc atgatggagg aaaacggcat agaattttta    840

aaaacaccag gatcatacta tgaatcccta tcatcaagga taggctcaat agacgaggat    900

ttaaatgaaa tagagaaaca taacatactt gtggatcgtg atgagaacgg atacctatta    960

cagatcttca caaagcctgt tactgacagg ccaacgttct tctttgaggt catacagaga   1020

aagggtgcaa ggtcattcgg caacggtaac tttaaggcac tttttgaggc gatagaaagg   1080

gagcaggcaa agagaggaaa cctatga                                       1107


<210>  20
<211>  368
<212>  PRT
<213>  Picrophilus torridus

<400>  20

Met Tyr Gly Lys Asn Leu Ile Ser Glu Leu Arg Glu Lys Glu Ile Phe
1               5                   10                  15


Lys Arg Leu His His Val Glu Phe Tyr Val Ser Ser Ala Lys Thr Trp
            20                  25                  30


Ser Tyr Phe Met Asn Arg Gly Leu Gly Phe Lys Thr Val Ala Tyr Ala
        35                  40                  45


Gly Pro Glu Thr Gly Ile Arg Asp Lys Ile Ser Tyr Val Met Ser Gln
    50                  55                  60


Gly Thr Ala Arg Ile Ser Phe Thr Ser Ser Met Asn Asp Asp Ser Tyr
65                  70                  75                  80


Ile Ser Asn His Val Lys Lys His Gly Asp Gly Val Lys Asp Ile Ala
```

```
                85                  90                  95

Leu Glu Val Asp Asp Leu Asp Glu Ala Lys Ser Leu Ile Glu Lys Tyr
            100                 105                 110

Gly Thr Lys Val Ser Lys Ile Asn Glu Ile Lys Asp Gly Asn Gly Lys
        115                 120                 125

Ile Arg Thr Ala Glu Ile Lys Thr Tyr Gly Glu Thr Val His Thr Leu
    130                 135                 140

Ile Glu Thr Gly Asp Tyr Asn Gly Val Phe Met Pro Gly Tyr Glu Glu
145                 150                 155                 160

Ser Glu Ile Asn Ser Lys Asn Thr Gly Ile Lys Lys Ile Asp His Ile
                165                 170                 175

Val Gly Asn Val Tyr Glu Gly Glu Met Asp Ser Trp Val Asn Phe Tyr
            180                 185                 190

Ile Glu Lys Leu Gly Phe Glu His Leu Ile Thr Phe Asp Asp Lys Asp
        195                 200                 205

Ile Arg Thr Asp Tyr Ser Ala Leu Arg Ser Lys Val Val Lys Tyr Asn
    210                 215                 220

Asp Asp Ile Val Phe Pro Ile Asn Glu Pro Ala Lys Gly Leu Arg Lys
225                 230                 235                 240

Ser Gln Ile Glu Glu Tyr Leu Asp Tyr Tyr Arg Ser Glu Gly Val Gln
                245                 250                 255

His Ile Ala Leu Leu Thr Asp Asp Ile Ile Lys Thr Val Ser Met Met
            260                 265                 270

Glu Glu Asn Gly Ile Glu Phe Leu Lys Thr Pro Gly Ser Tyr Tyr Glu
        275                 280                 285

Ser Leu Ser Ser Arg Ile Gly Ser Ile Asp Glu Asp Leu Asn Glu Ile
    290                 295                 300

Glu Lys His Asn Ile Leu Val Asp Arg Asp Glu Asn Gly Tyr Leu Leu
305                 310                 315                 320
```

```
Gln Ile Phe Thr Lys Pro Val Thr Asp Arg Pro Thr Phe Phe Phe Glu
                325                 330                 335


Val Ile Gln Arg Lys Gly Ala Arg Ser Phe Gly Asn Gly Asn Phe Lys
            340                 345                 350


Ala Leu Phe Glu Ala Ile Glu Arg Glu Gln Ala Lys Arg Gly Asn Leu
        355                 360                 365


<210>  21
<211>  1164
<212>  DNA
<213>  Kordia algicida

<400>  21
atggcagcag aaataaaaaa cttaaaagat ttacaaaata cagaatacgg actcaaaaaa      60

ttatttgacg aagcagaaga ctttcttcca cttttaggaa cagactacgt agaattatac     120

gtcgggaacg ccaaacaatc ggcacatttc tacaaaacgg cttttggttt tcaatcagaa     180

gcttacgcag gattggaaac aggattaacc gacagagttt catacgtatt aaaacaagat     240

aaaattcgct tggtcttaac aacaccatta ggaaaaggtg gcgaaatcaa tgagcatatc     300

gatttacacg gcgatggcgt aaaagtagta gcactttggg tagaagatgc tacaaaagcc     360

tttgaagaaa cgaccaaaag aggcgcaaaa ccgtacatgg aaccaacaaa agaagaagat     420

gaaaacggat atgtaattcg ctcaggaatc tatacgtacg gagaaacggt tcatgttttt     480

gtagaacgta aaaactataa cggagtcttt ttaccaggat atcaaagatg ggaatctcac     540

tacaatccgg agccagttgg cttaaaattc atcgatcaca tggtaggaaa tgtaggttgg     600

ggagaaatga aagaatggtg tgaattctac gcgaaagtaa tgggatttgc gcaaattatc     660

tcctttacag atgatgatat ttctaccgat tttactgcgt tgatgagtaa agtaatgagt     720

aatggaaatg gtagaatcaa atttccaatc aatgaacccg cagaaggaaa aaagaaatcg     780

caaattgaag aatatctaga cttttacaat ggttcaggag tacaacatat tgcggttgct     840

acagacaata ttattgatac ggtttcgcaa atgcgcgaac gtggagtaga attcttatac     900

gttccagata catattatga tgacttgtta gaacgtgttg gcgacatcga tgaagatgta     960

gaagaactca aaaaacacgg aatcttaatt gatcgtgatg aagaaggata cttattgcag    1020

ttatttacca aaccattgt agacagacca acaatgttct ttgaagtcat tcagcgtaaa    1080

ggcgcacaat catttggagt aggaaacttt aaagctttat ttgaagcgat agaaagagaa    1140

caagctgctc gcggaacatt gtaa                                           1164
```

```
<210>  22
<211>  387
<212>  PRT
<213>  Kordia algicida

<400>  22

Met Ala Ala Glu Ile Lys Asn Leu Lys Asp Leu Gln Asn Thr Glu Tyr
1               5                   10                  15


Gly Leu Lys Lys Leu Phe Asp Glu Ala Glu Asp Phe Leu Pro Leu Leu
            20                  25                  30


Gly Thr Asp Tyr Val Glu Leu Tyr Val Gly Asn Ala Lys Gln Ser Ala
        35                  40                  45


His Phe Tyr Lys Thr Ala Phe Gly Phe Gln Ser Glu Ala Tyr Ala Gly
    50                  55                  60


Leu Glu Thr Gly Leu Thr Asp Arg Val Ser Tyr Val Leu Lys Gln Asp
65                  70                  75                  80


Lys Ile Arg Leu Val Leu Thr Thr Pro Leu Gly Lys Gly Gly Glu Ile
                85                  90                  95


Asn Glu His Ile Asp Leu His Gly Asp Gly Val Lys Val Val Ala Leu
            100                 105                 110


Trp Val Glu Asp Ala Thr Lys Ala Phe Glu Glu Thr Thr Lys Arg Gly
        115                 120                 125


Ala Lys Pro Tyr Met Glu Pro Thr Lys Glu Glu Asp Glu Asn Gly Tyr
    130                 135                 140


Val Ile Arg Ser Gly Ile Tyr Thr Tyr Gly Glu Thr Val His Val Phe
145                 150                 155                 160


Val Glu Arg Lys Asn Tyr Asn Gly Val Phe Leu Pro Gly Tyr Gln Arg
                165                 170                 175


Trp Glu Ser His Tyr Asn Pro Glu Pro Val Gly Leu Lys Phe Ile Asp
            180                 185                 190


His Met Val Gly Asn Val Gly Trp Gly Glu Met Lys Glu Trp Cys Glu
        195                 200                 205
```

```
Phe Tyr Ala Lys Val Met Gly Phe Ala Gln Ile Ile Ser Phe Thr Asp
    210                 215                 220

Asp Asp Ile Ser Thr Asp Phe Thr Ala Leu Met Ser Lys Val Met Ser
225                 230                 235                 240

Asn Gly Asn Gly Arg Ile Lys Phe Pro Ile Asn Glu Pro Ala Glu Gly
                245                 250                 255

Lys Lys Lys Ser Gln Ile Glu Glu Tyr Leu Asp Phe Tyr Asn Gly Ser
            260                 265                 270

Gly Val Gln His Ile Ala Val Ala Thr Asp Asn Ile Ile Asp Thr Val
        275                 280                 285

Ser Gln Met Arg Glu Arg Gly Val Glu Phe Leu Tyr Val Pro Asp Thr
    290                 295                 300

Tyr Tyr Asp Asp Leu Leu Glu Arg Val Gly Asp Ile Asp Glu Asp Val
305                 310                 315                 320

Glu Glu Leu Lys Lys His Gly Ile Leu Ile Asp Arg Asp Glu Glu Gly
                325                 330                 335

Tyr Leu Leu Gln Leu Phe Thr Lys Thr Ile Val Asp Arg Pro Thr Met
            340                 345                 350

Phe Phe Glu Val Ile Gln Arg Lys Gly Ala Gln Ser Phe Gly Val Gly
        355                 360                 365

Asn Phe Lys Ala Leu Phe Glu Ala Ile Glu Arg Glu Gln Ala Ala Arg
    370                 375                 380

Gly Thr Leu
385


<210>  23
<211>  1323
<212>  DNA
<213>  Sorghum bicolor

<400>  23
atgcccccga cccccaccac agccgccgca accggcgccg ccgtggcggc ggcatcagcg      60

gagcaggcgg cgttccgcct cgtgggccac cgcaacttcg tccgcgtgaa cccgcgctcc     120

gaccgcttcc acacgctcgc gttccaccac gtggagctct ggtgcgccga cgcggcctcc     180
```

gccgcgggcc gcttctcctt cgggctcggc gcgccgctcg ccgcgcggtc cgacctctcc 240

acggggaaca ccgcgcacgc gtccctgctg ctccgctcgg gcgccctcgc gttcctcttc 300

acggcgccct acgcgcacgg cgccgacgcc gccacggcct cgctgccctc cttctccgcc 360

gccgaggcgc ggcgcttcgc ggccgaccac ggcctcgcgg tgcgcgccgt cgcgctccgc 420

gtggccgacg cggaggacgc cttccgcgcc agcgtcgcgg ccggcgcgcg cccggcgttc 480

gagcccgtcg agctcggcct cggcttccgc ctcgccgaag tcgagctcta cggcgacgtc 540

gtgctccggt acgtgagcta cccggacgac gcggacgcgt ccttcctgcc ggggttcgtg 600

ggcgtgacca gccccggcgc ggcggactac gggctgagga ggttcgacca catcgtcggc 660

aacgtgccgg agctggcgcc ggcggccgcc tacttcgctg gcttcacggg gttccacgag 720

ttcgccgagt tcacggcgga ggacgtgggc accacggaga gcgggctcaa ctcgatggtg 780

ctcgccaaca acgcggagaa cgtgctgctc ccactcaacg agccggtgca cggcaccaag 840

cgccgcagcc agatacagac gtacttggac caccacggcg gccccggcgt gcagcacatg 900

gcgctggcca gcgacgacgt gctcaggacg ctgagggaga tgcaagcgcg ctcggccatg 960

ggcggcttcg agttcatggc gcctccggcg cccgaatact atgacggcgt gaggcggcgc 1020

gccggggacg tgctcacgga ggcacagatt aaggagtgtc aggaactagg ggtgctggtg 1080

gacagagatg accagggcgt gctgctccag atcttcacca agccagtggg ggacaggcca 1140

acgttgttct tggagatcat tcaaaggatc gggtgcatgg agaaggatga gaaggggcaa 1200

gaataccaga agggtggctg tggcgggttt ggcaagggaa acttctccca gctgttcaaa 1260

tccattgagg attatgagaa gtcccttgaa gctaagcaag ctgcagcagc tcagggatcc 1320

tag 1323

<210> 24
<211> 440
<212> PRT
<213> Sorghum bicolor

<400> 24

```
Met Pro Pro Thr Pro Thr Thr Ala Ala Ala Thr Gly Ala Ala Val Ala
1               5                   10                  15


Ala Ala Ser Ala Glu Gln Ala Ala Phe Arg Leu Val Gly His Arg Asn
            20                  25                  30


Phe Val Arg Val Asn Pro Arg Ser Asp Arg Phe His Thr Leu Ala Phe
        35                  40                  45
```

```
His His Val Glu Leu Trp Cys Ala Asp Ala Ala Ser Ala Ala Gly Arg
    50                  55                  60

Phe Ser Phe Gly Leu Gly Ala Pro Leu Ala Ala Arg Ser Asp Leu Ser
65                  70                  75                  80

Thr Gly Asn Thr Ala His Ala Ser Leu Leu Leu Arg Ser Gly Ala Leu
                85                  90                  95

Ala Phe Leu Phe Thr Ala Pro Tyr Ala His Gly Ala Asp Ala Ala Thr
            100                 105                 110

Ala Ser Leu Pro Ser Phe Ser Ala Ala Glu Ala Arg Arg Phe Ala Ala
        115                 120                 125

Asp His Gly Leu Ala Val Arg Ala Val Ala Leu Arg Val Ala Asp Ala
    130                 135                 140

Glu Asp Ala Phe Arg Ala Ser Val Ala Ala Gly Ala Arg Pro Ala Phe
145                 150                 155                 160

Glu Pro Val Glu Leu Gly Leu Gly Phe Arg Leu Ala Glu Val Glu Leu
                165                 170                 175

Tyr Gly Asp Val Val Leu Arg Tyr Val Ser Tyr Pro Asp Asp Ala Asp
            180                 185                 190

Ala Ser Phe Leu Pro Gly Phe Val Gly Val Thr Ser Pro Gly Ala Ala
        195                 200                 205

Asp Tyr Gly Leu Arg Arg Phe Asp His Ile Val Gly Asn Val Pro Glu
    210                 215                 220

Leu Ala Pro Ala Ala Ala Tyr Phe Ala Gly Phe Thr Gly Phe His Glu
225                 230                 235                 240

Phe Ala Glu Phe Thr Ala Glu Asp Val Gly Thr Thr Glu Ser Gly Leu
                245                 250                 255

Asn Ser Met Val Leu Ala Asn Asn Ala Glu Asn Val Leu Leu Pro Leu
            260                 265                 270

Asn Glu Pro Val His Gly Thr Lys Arg Arg Ser Gln Ile Gln Thr Tyr
```

```
        275                 280                 285

Leu Asp His His Gly Gly Pro Gly Val Gln His Met Ala Leu Ala Ser
    290                 295                 300

Asp Asp Val Leu Arg Thr Leu Arg Glu Met Gln Ala Arg Ser Ala Met
305                 310                 315                 320

Gly Gly Phe Glu Phe Met Ala Pro Pro Ala Pro Glu Tyr Tyr Asp Gly
                325                 330                 335

Val Arg Arg Arg Ala Gly Asp Val Leu Thr Glu Ala Gln Ile Lys Glu
            340                 345                 350

Cys Gln Glu Leu Gly Val Leu Val Asp Arg Asp Asp Gln Gly Val Leu
        355                 360                 365

Leu Gln Ile Phe Thr Lys Pro Val Gly Asp Arg Pro Thr Leu Phe Leu
    370                 375                 380

Glu Ile Ile Gln Arg Ile Gly Cys Met Glu Lys Asp Glu Lys Gly Gln
385                 390                 395                 400

Glu Tyr Gln Lys Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser
                405                 410                 415

Gln Leu Phe Lys Ser Ile Glu Asp Tyr Glu Lys Ser Leu Glu Ala Lys
            420                 425                 430

Gln Ala Ala Ala Ala Gln Gly Ser
        435                 440


<210>  25
<211>  1311
<212>  DNA
<213>  Triticum aestivum

<400>  25
atgccgccca cccccaccac ccccgcagcc accggcgccg gcgctgccgc cgcggtgacg      60

ccggagcacg cgcggccgcg ccgaatggtc cgcttcaacc cgcgcagcga ccgcttccac     120

acgctctcct tccaccacgt cgagttctgg tgcgcggacg ccgcctccgc cgccggccgc     180

ttcgccttcg cgctcggcgc gccgctcgcc gccaggtccg acctctccac ggggaactcc     240

gtgcacgcct cccagctgct ccgctcgggc aacctcgcct tcctcttcac cgcgccctac     300
```

```
gcgaacggct gcgacgccgc caccgcctcc ctgccctcct tctccgccga cgccgcgcgc    360

cggttctccg cggaccacgg gctcgcagtg cgctccatag cactgcgcgt cgcagacgcc    420

gcagaggcct tccgcgccag cgtcgacgga ggcgcgcgcc cggccttcag ccccgtggac    480

ctcggccgcg gcttcggctt cgcggaggtc gagctctacg gcgacgtcgt gctccgcttc    540

gtcagtcacc cggatgacac ggacgtgccc ttcttgccgg ggttcgaggg cgtgagcaac    600

ccggatgccg tggactacgg cctgacgcgg ttcgaccacg tcgtcggcaa cgtcccggag    660

cttgcccccg ccgccgcata cgtcgccggg ttcgcggggt tccacgagtt cgccgagttc    720

acgacggagg acgtgggcac ggccgagagc gggctcaact cgatggtgct cgccaacaac    780

tcggagggcg tgctgctgcc gctcaacgag ccggtgcacg gcaccaagcg ccggagccag    840

atacagacgt tcctggaaca ccacggcggc tcgggcgtgc agcacatcgc ggtggccagc    900

agcgacgtgc tcaggacgct cagggagatg cgtgcgcgct ccgccatggg cggcttcgac    960

ttcctgccac cccgctgccg aaagtactac gaaggcgtgc ggcgcatcgc cggggatgtg   1020

ctctcggagg cgcagatcaa ggaatgccag gagctggggg tgctcgtcga cagggacgac   1080

caaggggtgt tgctacaaat cttcacaaag ccagtggggg acaggccaac gctgttcctg   1140

gagatgatcc aaaggatcgg gtgcatggag aaggacgaga gaggggaaga gtaccagaag   1200

ggtggctgcg gcgggttcgg caaaggcaac ttctccgagc tgttcaagtc cattgaagat   1260

tacgagaagt cccttgaagc caagcaatct gctgcagttc agggatcata g            1311


<210>  26
<211>  436
<212>  PRT
<213>  Triticum aestivum

<400>  26

Met Pro Pro Thr Pro Thr Thr Pro Ala Ala Thr Gly Ala Gly Ala Ala
1               5                   10                  15


Ala Ala Val Thr Pro Glu His Ala Arg Pro Arg Arg Met Val Arg Phe
            20                  25                  30


Asn Pro Arg Ser Asp Arg Phe His Thr Leu Ser Phe His His Val Glu
        35                  40                  45


Phe Trp Cys Ala Asp Ala Ala Ser Ala Ala Gly Arg Phe Ala Phe Ala
    50                  55                  60


Leu Gly Ala Pro Leu Ala Ala Arg Ser Asp Leu Ser Thr Gly Asn Ser
```

```
65                  70                  75                  80

Val His Ala Ser Gln Leu Leu Arg Ser Gly Asn Leu Ala Phe Leu Phe
                85                  90                  95

Thr Ala Pro Tyr Ala Asn Gly Cys Asp Ala Ala Thr Ala Ser Leu Pro
            100                 105                 110

Ser Phe Ser Ala Asp Ala Ala Arg Arg Phe Ser Ala Asp His Gly Leu
        115                 120                 125

Ala Val Arg Ser Ile Ala Leu Arg Val Ala Asp Ala Ala Glu Ala Phe
    130                 135                 140

Arg Ala Ser Val Asp Gly Gly Ala Arg Pro Ala Phe Ser Pro Val Asp
145                 150                 155                 160

Leu Gly Arg Gly Phe Gly Phe Ala Glu Val Glu Leu Tyr Gly Asp Val
                165                 170                 175

Val Leu Arg Phe Val Ser His Pro Asp Asp Thr Asp Val Pro Phe Leu
            180                 185                 190

Pro Gly Phe Glu Gly Val Ser Asn Pro Asp Ala Val Asp Tyr Gly Leu
        195                 200                 205

Thr Arg Phe Asp His Val Val Gly Asn Val Pro Glu Leu Ala Pro Ala
    210                 215                 220

Ala Ala Tyr Val Ala Gly Phe Ala Gly Phe His Glu Phe Ala Glu Phe
225                 230                 235                 240

Thr Thr Glu Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser Met Val
                245                 250                 255

Leu Ala Asn Asn Ser Glu Gly Val Leu Leu Pro Leu Asn Glu Pro Val
            260                 265                 270

His Gly Thr Lys Arg Arg Ser Gln Ile Gln Thr Phe Leu Glu His His
        275                 280                 285

Gly Gly Ser Gly Val Gln His Ile Ala Val Ala Ser Ser Asp Val Leu
    290                 295                 300
```

```
Arg Thr Leu Arg Glu Met Arg Ala Arg Ser Ala Met Gly Gly Phe Asp
305                 310                 315                 320


Phe Leu Pro Pro Arg Cys Arg Lys Tyr Tyr Glu Gly Val Arg Arg Ile
                325                 330                 335


Ala Gly Asp Val Leu Ser Glu Ala Gln Ile Lys Glu Cys Gln Glu Leu
            340                 345                 350


Gly Val Leu Val Asp Arg Asp Asp Gln Gly Val Leu Leu Gln Ile Phe
        355                 360                 365


Thr Lys Pro Val Gly Asp Arg Pro Thr Leu Phe Leu Glu Met Ile Gln
    370                 375                 380


Arg Ile Gly Cys Met Glu Lys Asp Glu Arg Gly Glu Glu Tyr Gln Lys
385                 390                 395                 400


Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu Phe Lys
                405                 410                 415


Ser Ile Glu Asp Tyr Glu Lys Ser Leu Glu Ala Lys Gln Ser Ala Ala
            420                 425                 430


Val Gln Gly Ser
        435


<210>  27
<211>  1305
<212>  DNA
<213>  Hordeum vulgare

<400>  27
atgccgccca cccccaccac ccccgcggct accggcgccg ccgccgcggt gacgccggag      60

cacgcgcgac cgcaccgaat ggtccgcttc aacccgcgca gcgaccgctt ccacacgctc     120

tccttccacc acgtcgagtt ctggtgcgcg gacgccgcct ccgccgccgg ccgcttcgcg     180

ttcgcgctcg gcgcgccgct cgccgccagg tccgacctct ccacggggaa ctccgcgcac     240

gcctcccagc tgctccgctc gggctccctc gccttcctct tcaccgcgcc ctacgccaac     300

ggctgcgacg ccgccaccgc ctccctgccc tccttctccg ccgacgccgc gcgccggttc     360

tccgccgacc acgggatcgc ggtgcgctcc gtagcgctgc gcgtcgcaga cgccgccgag     420

gccttccgcg ccagtcgtcg acggggcgcg cgcccggcct tcgcccccgt ggacctcggc     480

cgcggcttcg cgttcgcgga ggtcgagctc tacggcgacg tcgtgctccg cttcgtcagc     540
```

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cacccggacg gcacggacgt gcccttcttg ccggggttcg agggcgtaac caacccggac     600

gccgtggact acggcctgac gcggttcgac cacgtcgtcg gcaacgtccc ggagcttgcc     660

cccgccgcag cctacatcgc cgggttcacg gggttccacg agttcgccga gttcacggcg     720

gaggacgtgg gcacgaccga gagcgggctc aactcggtgg tgctcgccaa caactcggag     780

ggcgtgctgc tgccgctcaa cgagccggtg cacggcacca agcgccggag ccagatacag     840

acgttcctgg aacaccacgg cggcccgggc gtgcagcaca tcgcggtggc cagcagtgac     900

gtgctcagga cgctcaggaa gatgcgtgcg cgctccgcca tgggcggctt cgacttcctg     960

ccacccccgc tgccgaagta ctacgaaggc gtgcgacgcc ttgccgggga tgtcctctcg    1020

gaggcgcaga tcaaggaatg ccaggagctg ggtgtgctcg tcgataggga cgaccaaggg    1080

gtgttgctcc aaatcttcac caagccagta ggggacaggc cgaccttgtt cctggagatg    1140

atccagagga tcgggtgcat ggagaaggac gagagagggg aagagtacca gaagggtggc    1200

tgcggcgggt tcggcaaagg caacttctcc gagctgttca agtccattga agattacgag    1260

aagtcccttg aagccaagca atctgctgca gttcagggat catag                    1305


<210>  28
<211>  434
<212>  PRT
<213>  Hordeum vulgare

<400>  28

Met Pro Pro Thr Pro Thr Thr Pro Ala Ala Thr Gly Ala Ala Ala Ala
1               5                   10                  15


Val Thr Pro Glu His Ala Arg Pro His Arg Met Val Arg Phe Asn Pro
            20                  25                  30


Arg Ser Asp Arg Phe His Thr Leu Ser Phe His His Val Glu Phe Trp
        35                  40                  45


Cys Ala Asp Ala Ala Ser Ala Ala Gly Arg Phe Ala Phe Ala Leu Gly
    50                  55                  60


Ala Pro Leu Ala Ala Arg Ser Asp Leu Ser Thr Gly Asn Ser Ala His
65                  70                  75                  80


Ala Ser Gln Leu Leu Arg Ser Gly Ser Leu Ala Phe Leu Phe Thr Ala
                85                  90                  95
```

```
Pro Tyr Ala Asn Gly Cys Asp Ala Ala Thr Ala Ser Leu Pro Ser Phe
            100                 105                 110

Ser Ala Asp Ala Ala Arg Arg Phe Ser Ala Asp His Gly Ile Ala Val
        115                 120                 125

Arg Ser Val Ala Leu Arg Val Ala Asp Ala Ala Glu Ala Phe Arg Ala
    130                 135                 140

Ser Arg Arg Arg Gly Ala Arg Pro Ala Phe Ala Pro Val Asp Leu Gly
145                 150                 155                 160

Arg Gly Phe Ala Phe Ala Glu Val Glu Leu Tyr Gly Asp Val Val Leu
                165                 170                 175

Arg Phe Val Ser His Pro Asp Gly Thr Asp Val Pro Phe Leu Pro Gly
            180                 185                 190

Phe Glu Gly Val Thr Asn Pro Asp Ala Val Asp Tyr Gly Leu Thr Arg
        195                 200                 205

Phe Asp His Val Val Gly Asn Val Pro Glu Leu Ala Pro Ala Ala Ala
    210                 215                 220

Tyr Ile Ala Gly Phe Thr Gly Phe His Glu Phe Ala Glu Phe Thr Ala
225                 230                 235                 240

Glu Asp Val Gly Thr Thr Glu Ser Gly Leu Asn Ser Val Val Leu Ala
                245                 250                 255

Asn Asn Ser Glu Gly Val Leu Leu Pro Leu Asn Glu Pro Val His Gly
            260                 265                 270

Thr Lys Arg Arg Ser Gln Ile Gln Thr Phe Leu Glu His His Gly Gly
        275                 280                 285

Pro Gly Val Gln His Ile Ala Val Ala Ser Ser Asp Val Leu Arg Thr
    290                 295                 300

Leu Arg Lys Met Arg Ala Arg Ser Ala Met Gly Gly Phe Asp Phe Leu
305                 310                 315                 320

Pro Pro Pro Leu Pro Lys Tyr Tyr Glu Gly Val Arg Arg Leu Ala Gly
                325                 330                 335
```

```
Asp Val Leu Ser Glu Ala Gln Ile Lys Glu Cys Gln Glu Leu Gly Val
            340                 345                 350

Leu Val Asp Arg Asp Asp Gln Gly Val Leu Leu Gln Ile Phe Thr Lys
        355                 360                 365

Pro Val Gly Asp Arg Pro Thr Leu Phe Leu Glu Met Ile Gln Arg Ile
    370                 375                 380

Gly Cys Met Glu Lys Asp Glu Arg Gly Glu Glu Tyr Gln Lys Gly Gly
385                 390                 395                 400

Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu Phe Lys Ser Ile
                405                 410                 415

Glu Asp Tyr Glu Lys Ser Leu Glu Ala Lys Gln Ser Ala Ala Val Gln
            420                 425                 430

Gly Ser


<210>  29
<211>  1209
<212>  DNA
<213>  Rhodococcus sp.

<400>  29
atgactaccg ccgacattcg cctgacgccc cgcgaggtgg ccgcacatct ggagaccgac      60

gagctccggc agttggtcgg gctcgtcgaa cacgacgacg cgtcggatcc gtttcccgtg     120

gtcgcgatgg atgccgtggt gttcgtgtgc ggcaacgcga cgcagagcac gcagtacttc     180

gtctccacgt ggggcatgac cctcgtcgcc tacgccgggc cggagaccgg tcagcgctcg     240

cacaagtcct tcgtcctcga gtcggggtcg gcacggttcg tgctgcacgg cgccgtcgat     300

ccgaagagcc cgctcgcgga ccatcaccgg gcgcacggcg acggcgtggt ggacctggcg     360

atggaagttc tcgacgtcga ccgctgcatc gcgcatgcac gctcgcaggg ggccaccatt     420

ctcgaggagc cgcgcgacgt cacggatcag ttcggcaccg tgcggctcgc ggcgatcgcc     480

acgtacggca gcacccggca caccatcgtc gaccgaagcc gatacgacgg cccctacctc     540

cccggattcg tcgcgcgctc cagcggtttc gcggcgcgac cgggtaaacc cccgcgattg     600

ttccaggcgc tcgaccacgc cgtcggcaac gtcgagatgg gccggatgga tcactgggtc     660

cggttctaca accgcgtcat gggcttcacg aacatggccg aattcgtcgg cgacgacatc     720
```

```
gccacggagt actcggcgct gatgtcgaag gtcgtggcga acggcaatca ccgggtgaag     780

ttcccgctca acgaacccgc ggtgggaaag aagaagtcgc agatcgacga atatctcgag     840

ttctacggtg agccgggctg ccagcatctg gccctcgcga ccggagacat cctcgcgacg     900

gtggacgcgt tgcgggccga gggtgtcgaa ttcctgaaca cacccgacgc gtactacgag     960

gacccacagc tgcgcgcccg gatcggcagg gtgcgggtgc cggtggagga actgcagaag    1020

cgcggaatcc tcgtcgaccg cgacgaggac ggatacctcc tgcagatctt caccaaaccg    1080

ctcggcgacc ggccgaccgt gttcttcgag gtgatcgaac ggcacggttc gctcgggttc    1140

ggggcgggta acttccaggc cctgttcgaa tccatcgagc gtgagcaggc ggcgcgcggc    1200

aatctgtga                                                            1209


<210>  30
<211>  402
<212>  PRT
<213>  Rhodococcus sp.

<400>  30

Met Thr Thr Ala Asp Ile Arg Leu Thr Pro Arg Glu Val Ala Ala His
1               5                   10                  15


Leu Glu Thr Asp Glu Leu Arg Gln Leu Val Gly Leu Val Glu His Asp
            20                  25                  30


Asp Ala Ser Asp Pro Phe Pro Val Val Ala Met Asp Ala Val Val Phe
        35                  40                  45


Val Cys Gly Asn Ala Thr Gln Ser Thr Gln Tyr Phe Val Ser Thr Trp
    50                  55                  60


Gly Met Thr Leu Val Ala Tyr Ala Gly Pro Glu Thr Gly Gln Arg Ser
65                  70                  75                  80


His Lys Ser Phe Val Leu Glu Ser Gly Ser Ala Arg Phe Val Leu His
                85                  90                  95


Gly Ala Val Asp Pro Lys Ser Pro Leu Ala Asp His His Arg Ala His
            100                 105                 110


Gly Asp Gly Val Val Asp Leu Ala Met Glu Val Leu Asp Val Asp Arg
        115                 120                 125


Cys Ile Ala His Ala Arg Ser Gln Gly Ala Thr Ile Leu Glu Glu Pro
```

```
        130                 135                 140

Arg Asp Val Thr Asp Gln Phe Gly Thr Val Arg Leu Ala Ala Ile Ala
145                 150                 155                 160

Thr Tyr Gly Ser Thr Arg His Thr Ile Val Asp Arg Ser Arg Tyr Asp
                165                 170                 175

Gly Pro Tyr Leu Pro Gly Phe Val Ala Arg Ser Ser Gly Phe Ala Ala
            180                 185                 190

Arg Pro Gly Lys Pro Pro Arg Leu Phe Gln Ala Leu Asp His Ala Val
        195                 200                 205

Gly Asn Val Glu Met Gly Arg Met Asp His Trp Val Arg Phe Tyr Asn
    210                 215                 220

Arg Val Met Gly Phe Thr Asn Met Ala Glu Phe Val Gly Asp Asp Ile
225                 230                 235                 240

Ala Thr Glu Tyr Ser Ala Leu Met Ser Lys Val Val Ala Asn Gly Asn
                245                 250                 255

His Arg Val Lys Phe Pro Leu Asn Glu Pro Ala Val Gly Lys Lys Lys
            260                 265                 270

Ser Gln Ile Asp Glu Tyr Leu Glu Phe Tyr Gly Glu Pro Gly Cys Gln
        275                 280                 285

His Leu Ala Leu Ala Thr Gly Asp Ile Leu Ala Thr Val Asp Ala Leu
    290                 295                 300

Arg Ala Glu Gly Val Glu Phe Leu Asn Thr Pro Asp Ala Tyr Tyr Glu
305                 310                 315                 320

Asp Pro Gln Leu Arg Ala Arg Ile Gly Arg Val Arg Val Pro Val Glu
                325                 330                 335

Glu Leu Gln Lys Arg Gly Ile Leu Val Asp Arg Asp Glu Asp Gly Tyr
            340                 345                 350

Leu Leu Gln Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Val Phe
        355                 360                 365
```

```
Phe Glu Val Ile Glu Arg His Gly Ser Leu Gly Phe Gly Ala Gly Asn
    370                 375                 380


Phe Gln Ala Leu Phe Glu Ser Ile Glu Arg Glu Gln Ala Ala Arg Gly
385                 390                 395                 400


Asn Leu



<210>  31
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  Nucleic acid sequence encoding Arabidopsis HPPD plus containing
       at the 5' end a nucleic acid encoding an Ala and 6 His amino
       acids


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for an Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding for an His Tag containing 6 His

<400>  31
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat      60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat ttccaagtt cgtaagaaag      120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc     180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa     240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc     300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca     360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat     420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc     480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg     540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa     600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc     660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt     720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca     780
```

```
gacgacgttg gaaccgccga gagcggttta aattcagcgg tcctggctag caatgatgaa    840

atggttcttc taccgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag    900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac    960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg   1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc   1080

gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg   1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata   1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga   1260

tgtggtggtt ttggcaaagg caatttctct gagctcttca agtccattga agaatacgaa   1320

aagactcttg aagccaaaca gttagtggga tga                                1353


<210>  32
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 31


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  32

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15


Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30


Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45


Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60
```

```
Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80

Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95

Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110

Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125

Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140

Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270

Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300
```

```
His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380

Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400

Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415

Gln Ser Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu
            420                 425                 430

Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445

Val Gly
    450


<210>  33
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  nucleotide sequence encoding mutant HPPD polypeptide


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding an His Tag containing 6 His
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<400>  33
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat      60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat tttccaagtt cgtaagaaag     120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc     180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa     240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc     300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca     360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat     420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc     480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg     540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa     600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc     660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt     720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca     780

gacgacgttg gaaccgccga gagcggttta aatgcggcgg tcctggctag caatgatgaa     840

atggttcttc taccgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag     900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac     960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg    1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc    1080

gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg    1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata    1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga    1260

tgtggtggtt ttggcaaagg caatttctct gagctcttca agtccattga agaatacgaa    1320

aagactcttg aagccaaaca gttagtggga tga                                 1353


<210>  34
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 33


<220>
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```
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  34

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15


Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30


Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45


Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60


Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80


Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95


Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110


Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125


Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140


Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160


Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175


Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190
```

```
Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ala
            260                 265                 270

Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380

Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400

Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415

Gln Ser Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu
            420                 425                 430
```

```
Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445


Val Gly
    450


<210>  35
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  nucleotide sequence encoding mutant HPPD polypeptide


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding for an His Tag containing 6 His

<400>  35
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat      60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat ttccaagtt  cgtaagaaag     120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc     180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa     240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc     300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca     360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat     420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc     480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg     540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa     600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc     660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt     720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca     780

gacgacgttg gaaccgccga gagcggttta aattcagcgg tcctggctag caatgatgaa     840

atggttcttc taccgattgc cgagccagtg cacggaacaa agaggaagag tcagattcag     900
```

```
acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac     960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg    1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc    1080

gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg    1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata    1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga    1260

tgtggtggtt ttggcaaagg caatttctct gagctcttca agtccattga agaatacgaa    1320

aagactcttg aagccaaaca gttagtggga tga                                  1353


<210>  36
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 35


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  36

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15


Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30


Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45


Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60


Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80


Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
```

```
                85                  90                  95

Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110

Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125

Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140

Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270

Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Ala Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320
```

```
Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380

Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400

Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415

Gln Ser Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu
            420                 425                 430

Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445

Val Gly
    450


<210>  37
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  nucleotide sequence encoding mutant HPPD polypeptide


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding for an His Tag containing 6 His

<400>  37
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat      60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat tttccaagtt cgtaagaaag     120
```

```
aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc    180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa    240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc    300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca    360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat    420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc    480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg    540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa    600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc    660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt    720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcatc tttcacagca    780

gacgacgttg gaaccgccga gagcggttta aattcagcgg tcctggctag caatgatgaa    840

atggttcttc taccgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag    900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac    960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg   1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc   1080

gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg   1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata   1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga   1260

tgtggtggtt ttggcaaagg caatttctct gagctcttca agtccattga agaatacgaa   1320

aagactcttg aagccaaaca gttagtggga tga                                 1353


<210>  38
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 37


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
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```
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  38

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15

Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30

Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45

Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60

Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80

Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95

Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110

Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125

Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140

Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
```

```
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Ser Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270

Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380

Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400

Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415

Gln Ser Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu
            420                 425                 430

Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445
```

```
Val Gly
    450


<210>  39
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  nucleotide sequence encoding mutant HPPD polypeptide


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding for an His Tag containing 6 His

<400>  39
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat      60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat tttccaagtt cgtaagaaag     120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc     180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa     240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc     300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca     360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat     420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc     480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg     540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa     600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc     660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt     720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca     780

gacgacgttg gaaccgccga gagcggttta aattcagcgg cgctggctag caatgatgaa     840

atggttcttc taccgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag     900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac     960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg    1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc    1080
```

```
gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg   1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata   1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga   1260

tgtggtggtt ttggcaaagg caatttctct gagctcttca agtccattga agaatacgaa   1320

aagactcttg aagccaaaca gttagtggga tga                                1353


<210>  40
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 39


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  40

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15


Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30


Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45


Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60


Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80


Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95


Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110
```

```
Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125

Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140

Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270

Ala Ala Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
```

```
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380

Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400

Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415

Gln Ser Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu
            420                 425                 430

Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445

Val Gly
    450


<210>  41
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  nucleotide sequebc encoding mutant HPPD polypeptide


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding for an His Tag containing 6 His

<400>  41
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat      60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat tttccaagtt cgtaagaaag     120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc     180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa     240
```

```
tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc    300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca    360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat    420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc    480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg    540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa    600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc    660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt    720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca    780

gacgacgttg gaaccgccga gagcggttta aattcagcgg tcctggctag caatgatgaa    840

atggttcttc tagcgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag    900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac    960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg   1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc   1080

gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg   1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata   1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga   1260

tgtggtggtt ttggcaaagg caatttctct gagctcttca agtccattga agaatacgaa   1320

aagactcttg aagccaaaca gttagtggga tga                                1353


<210>  42
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 41


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  42
```

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Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15

Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30

Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45

Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60

Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80

Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95

Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110

Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125

Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140

Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240
```

```
Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270

Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Ala Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380

Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400

Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415

Gln Ser Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu
            420                 425                 430

Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445

Val Gly
    450

<210>  43
```

```
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  nucleotide sequence encoding mutant HPPD polypeptide


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding for an His Tag containing 6 His

<400>  43
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat     60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat ttccaagtt cgtaagaaag    120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc    180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa    240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc    300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca    360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat    420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc    480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg    540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa    600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc    660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt    720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca    780

gacgacgttg gaaccgccga gagcggttta aattcagcgg tcctggctag caatgatgaa    840

atggttcttc taccgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag    900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac    960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg   1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc   1080

gatgatcaga tcaaggagtg tgaggaatta gggattatgg tagacagaga tgatcaaggg   1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata   1200
```

```
atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga   1260

tgtggtggtt ttggcaaagg caatttctct gagctcttca agtccattga agaatacgaa   1320

aagactcttg aagccaaaca gttagtggga tga                                 1353


<210>  44
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 43


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  44

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15


Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30


Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45


Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60


Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80


Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95


Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110


Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125
```

```
Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140

Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270

Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365
```

```
Glu Leu Gly Ile Met Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380


Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400


Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415


Gln Ser Gly Gly Cys Gly Gly Phe Gly Lys Gly Asn Phe Ser Glu Leu
            420                 425                 430


Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445


Val Gly
    450


<210>  45
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  nucleotide sequence encoding mutant HPPD polypeptide


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding for an His Tag containing 6 His

<400>  45
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat      60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat tttccaagtt cgtaagaaag     120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc     180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa     240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc     300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca     360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat     420
```

```
ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc    480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg    540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa    600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc    660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt    720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca    780

gacgacgttg gaaccgccga gagcggttta aattcagcgg tcctggctag caatgatgaa    840

atggttcttc taccgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag    900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac    960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg   1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc   1080

gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg   1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata   1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga   1260

tgtggtggtt ttggcattgg caatttctct gagctcttca agtccattga agaatacgaa   1320

aagactcttg aagccaaaca gttagtggga tga                                1353


<210>  46
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 45


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  46

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15
```

```
Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30

Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45

Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60

Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80

Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95

Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110

Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125

Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140

Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255
```

```
Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270

Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380

Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400

Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415

Gln Ser Gly Gly Cys Gly Gly Phe Gly Ile Gly Asn Phe Ser Glu Leu
            420                 425                 430

Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445

Val Gly
    450


<210>  47
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
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<223> nucleotide sequence encoding mutant HPPD polypeptide

<220>
<221> misc_feature
<222> (4)..(6)
<223> sequence coding for Ala

<220>
<221> misc_feature
<222> (7)..(24)
<223> sequence coding for an His Tag containing 6 His

<400> 47
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat 60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat ttccaagtt cgtaagaaag 120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc 180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa 240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc 300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca 360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat 420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc 480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg 540

atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa 600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc 660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt 720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca 780

gacgacgttg gaaccgccga gagcggttta aattcagcgg tcctggctag caatgatgaa 840

atggttcttc taccgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag 900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac 960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg 1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc 1080

gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg 1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata 1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga 1260

tgtggtggtt ttggccaggg caatttctct gagctcttca agtccattga agaatacgaa 1320

aagactcttg aagccaaaca gttagtggga tga 1353

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<210>  48
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 47


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  48

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15


Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30


Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
        35                  40                  45


Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60


Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80


Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95


Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110


Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125


Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140
```

```
Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270

Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380
```

```
Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400


Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415


Gln Ser Gly Gly Cys Gly Gly Phe Gly Gln Gly Asn Phe Ser Glu Leu
            420                 425                 430


Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445


Val Gly
    450


<210>  49
<211>  1353
<212>  DNA
<213>  Artificial sequence

<220>
<223>  nucleotide sequence encoding mutant HPPD polypeptide


<220>
<221>  misc_feature
<222>  (4)..(6)
<223>  sequence coding for Ala

<220>
<221>  misc_feature
<222>  (7)..(24)
<223>  sequence coding for an His Tag containing 6 His

<400>  49
atggctcatc accatcacca tcaccaaaac gccgccgttt cagagaatca aaaccatgat      60

gacggcgctg cgtcgtcgcc gggattcaag ctcgtcggat ttccaagtt cgtaagaaag      120

aatccaaagt ctgataaatt caaggttaag cgcttccatc acatcgagtt ctggtgcggc     180

gacgcaacca acgtcgctcg tcgcttctcc tggggtctgg ggatgagatt ctccgccaaa     240

tccgatcttt ccaccggaaa catggttcac gcctcttacc tactcacctc cggtgacctc     300

cgattccttt tcactgctcc ttactctccg tctctctccg ccggagagat taaaccgaca     360

accacagctt ctatcccaag tttcgatcac ggctcttgtc gttccttctt ctcgtcacat     420

ggtctcggtg ttagagccgt tgcgattgaa gtagaagacg cagagtcagc tttctccatc     480

agtgtagcta atggcgctat tccttcgtcg cctcctatcg tcctcaatga agcagttacg     540
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```
atcgctgagg ttaaactata cggcgatgtt gttctccgat atgttagtta caaagcagaa    600

gataccgaaa aatccgaatt cttgccaggg ttcgagcgtg tagaggatgc gtcgtcgttc    660

ccattggatt atggtatccg gcggcttgac cacgccgtgg gaaacgttcc tgagcttggt    720

ccggctttaa cttatgtagc ggggttcact ggttttcacc aattcgcaga gttcacagca    780

gacgacgttg gaaccgccga gagcggttta aattcagcgg tcctggctag caatgatgaa    840

atggttcttc taccgattaa cgagccagtg cacggaacaa agaggaagag tcagattcag    900

acgtatttgg aacataacga aggcgcaggg ctacaacatc tggctctgat gagtgaagac    960

atattcagga ccctgagaga gatgaggaag aggagcagta ttggaggatt cgacttcatg   1020

ccttctcctc cgcctactta ctaccagaat ctcaagaaac gggtcggcga cgtgctcagc   1080

gatgatcaga tcaaggagtg tgaggaatta gggattcttg tagacagaga tgatcaaggg   1140

acgttgcttc aaatcttcac aaaaccacta ggtgacaggc cgacgatatt tatagagata   1200

atccagagag taggatgcat gatgaaagat gaggaaggga aggcttacca gagtggagga   1260

tgtggtggtt ttggcgtggg caatttctct gagctcttca agtccattga agaatacgaa   1320

aagactcttg aagccaaaca gttagtggga tga                                1353


<210>  50
<211>  450
<212>  PRT
<213>  Artificial sequence

<220>
<223>  encoded by SEQ ID No. 49


<220>
<221>  MISC_FEATURE
<222>  (2)..(2)
<223>  Ala

<220>
<221>  MISC_FEATURE
<222>  (3)..(8)
<223>  His Tag made of 6 His

<400>  50

Met Ala His His His His His His Gln Asn Ala Ala Val Ser Glu Asn
1               5                   10                  15


Gln Asn His Asp Asp Gly Ala Ala Ser Ser Pro Gly Phe Lys Leu Val
            20                  25                  30


Gly Phe Ser Lys Phe Val Arg Lys Asn Pro Lys Ser Asp Lys Phe Lys
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        35                  40                  45

Val Lys Arg Phe His His Ile Glu Phe Trp Cys Gly Asp Ala Thr Asn
    50                  55                  60

Val Ala Arg Arg Phe Ser Trp Gly Leu Gly Met Arg Phe Ser Ala Lys
65                  70                  75                  80

Ser Asp Leu Ser Thr Gly Asn Met Val His Ala Ser Tyr Leu Leu Thr
                85                  90                  95

Ser Gly Asp Leu Arg Phe Leu Phe Thr Ala Pro Tyr Ser Pro Ser Leu
            100                 105                 110

Ser Ala Gly Glu Ile Lys Pro Thr Thr Thr Ala Ser Ile Pro Ser Phe
        115                 120                 125

Asp His Gly Ser Cys Arg Ser Phe Phe Ser Ser His Gly Leu Gly Val
    130                 135                 140

Arg Ala Val Ala Ile Glu Val Glu Asp Ala Glu Ser Ala Phe Ser Ile
145                 150                 155                 160

Ser Val Ala Asn Gly Ala Ile Pro Ser Ser Pro Pro Ile Val Leu Asn
                165                 170                 175

Glu Ala Val Thr Ile Ala Glu Val Lys Leu Tyr Gly Asp Val Val Leu
            180                 185                 190

Arg Tyr Val Ser Tyr Lys Ala Glu Asp Thr Glu Lys Ser Glu Phe Leu
        195                 200                 205

Pro Gly Phe Glu Arg Val Glu Asp Ala Ser Ser Phe Pro Leu Asp Tyr
    210                 215                 220

Gly Ile Arg Arg Leu Asp His Ala Val Gly Asn Val Pro Glu Leu Gly
225                 230                 235                 240

Pro Ala Leu Thr Tyr Val Ala Gly Phe Thr Gly Phe His Gln Phe Ala
                245                 250                 255

Glu Phe Thr Ala Asp Asp Val Gly Thr Ala Glu Ser Gly Leu Asn Ser
            260                 265                 270
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Ala Val Leu Ala Ser Asn Asp Glu Met Val Leu Leu Pro Ile Asn Glu
        275                 280                 285

Pro Val His Gly Thr Lys Arg Lys Ser Gln Ile Gln Thr Tyr Leu Glu
    290                 295                 300

His Asn Glu Gly Ala Gly Leu Gln His Leu Ala Leu Met Ser Glu Asp
305                 310                 315                 320

Ile Phe Arg Thr Leu Arg Glu Met Arg Lys Arg Ser Ser Ile Gly Gly
                325                 330                 335

Phe Asp Phe Met Pro Ser Pro Pro Pro Thr Tyr Tyr Gln Asn Leu Lys
            340                 345                 350

Lys Arg Val Gly Asp Val Leu Ser Asp Asp Gln Ile Lys Glu Cys Glu
        355                 360                 365

Glu Leu Gly Ile Leu Val Asp Arg Asp Asp Gln Gly Thr Leu Leu Gln
    370                 375                 380

Ile Phe Thr Lys Pro Leu Gly Asp Arg Pro Thr Ile Phe Ile Glu Ile
385                 390                 395                 400

Ile Gln Arg Val Gly Cys Met Met Lys Asp Glu Glu Gly Lys Ala Tyr
                405                 410                 415

Gln Ser Gly Gly Cys Gly Gly Phe Gly Val Gly Asn Phe Ser Glu Leu
            420                 425                 430

Phe Lys Ser Ile Glu Glu Tyr Glu Lys Thr Leu Glu Ala Lys Gln Leu
        435                 440                 445

Val Gly
    450
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Claims

1. An isolated nucleic acid comprising a nucleotide sequence encoding a mutated HPPD protein,
wherein said mutated HPPD protein has HPPD activity, and
wherein in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises at least one amino acid selected from:

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at a position in an HPPD protein, said position corresponding to position 250 of the amino acid sequence of SEQ ID No. 2;
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at a position in an HPPD protein, said position corresponding to position 251 of the amino acid sequence of SEQ ID No. 2;

c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 2;
d) Ala, Phe, His, Gln, Val or Trp at a position in an HPPD protein, said position corresponding to position 253 of the amino acid sequence of SEQ ID No. 2;
e) Leu or Val at a position in an HPPD protein, said position corresponding to position 265 of the amino acid sequence of SEQ ID No. 2;
f) Leu, Gln, Arg, Val or Tyr at a position in an HPPD protein, said position corresponding to position 268 of the amino acid sequence of SEQ ID No. 2;
g) Ala, Thr or Val at a position in an HPPD protein, said position corresponding to position 269 of the amino acid sequence of SEQ ID No. 2;
h) Ala, Ile, Asn, Pro, Thr or Val at a position in an HPPD protein, said position corresponding to position 280 of the amino acid sequence of SEQ ID No. 2;
i) Leu, Gln or Val at a position in an HPPD protein, said position corresponding to position 293 of the amino acid sequence of SEQ ID No. 2;
j) Ile or Met at a position in an HPPD protein, said position corresponding to position 294 of the amino acid sequence of SEQ ID No. 2;
k) Gln at a position in an HPPD protein, said position corresponding to position 307 of the amino acid sequence of SEQ ID No. 2;
l) Ile, Met or Asn at a position in an HPPD protein, said position corresponding to position 335 of the amino acid sequence of SEQ ID No. 2;
m) Leu at a position in an HPPD protein, said position corresponding to position 368 of the amino acid sequence of SEQ ID No. 2;
n) Phe or Tyr at a position in an HPPD protein, said position corresponding to position 381 of the amino acid sequence of SEQ ID No. 2;
o) Phe or Ser at a position in an HPPD protein, said position corresponding to position 392 of the amino acid sequence of SEQ ID No. 2;
p) Phe or Tyr at a position in an HPPD protein, said position corresponding to position 419 of the amino acid sequence of SEQ ID No. 2;
q) Asp, Lys or Asn at a position in an HPPD protein, said position corresponding to position 421 of the amino acid sequence of SEQ ID No. 2;
r) Ala, Gly, Met, Pro or Thr at a position in an HPPD protein, said position corresponding to position 422 of the amino acid sequence of SEQ ID No. 2;
s) Ala, Phe, Ile or Val at a position in an HPPD protein, said position corresponding to position 424 of the amino acid sequence of SEQ ID No. 2;
t) Ile, Pro, Arg or Ser at a position in an HPPD protein, said position corresponding to position 425 of the amino acid sequence of SEQ ID No. 2;
u) Glu, Phe, Thr or Val at a position in an HPPD protein, said position corresponding to position 426 of the amino acid sequence of SEQ ID No. 2;
v) Ile, Met, Gln or Val at a position in an HPPD protein, said position corresponding to position 431 of the amino acid sequence of SEQ ID No. 2; and
w) at least one amino acid deletion or replacement at any one of positions 228, 248, 270, 271, 379 and/or 427.

2. The isolated nucleic acid of claim 1, wherein said at least one amino acid is selected from

a) Ala, Asp, Glu, Phe, Thr, Val or Tyr at a position in an HPPD protein, said position corresponding to position 250 of the amino acid sequence of SEQ ID No. 2;
b) Ala, Asp, Glu, Ile, Lys, Leu, Pro or Arg at a position in an HPPD protein, said position corresponding to position 251 of the amino acid sequence of SEQ ID No. 2;
c) Glu, Thr, Arg, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 2;
d) Ala, Phe, Val or Trp at a position in an HPPD protein, said position corresponding to position 253 of the amino acid sequence of SEQ ID No. 2;
e) Leu or Val at a position in an HPPD protein, said position corresponding to position 265 of the amino acid sequence of SEQ ID No. 2;
f) Leu, Gln, Arg, Val or Tyr at a position in an HPPD protein, said position corresponding to position 268 of the amino acid sequence of SEQ ID NO: 2;
g) Ala or Val at a position in an HPPD protein, said position corresponding to position 269 of the amino acid sequence of SEQ ID No. 2;

h) Ala, Pro, Thr or Val at a position in an HPPD protein, said position corresponding to position 280 of the amino acid sequence of SEQ ID No. 2;
i) Gln at a position in an HPPD protein, said position corresponding to position 307 of the amino acid sequence of SEQ ID No. 2;
j) Ile or Met at a position in an HPPD protein, said position corresponding to position 335 of the amino acid sequence of SEQ ID No. 2;
k) Leu at a position in an HPPD protein, said position corresponding to position 368 of the amino acid sequence of SEQ ID No. 2;
l) Phe at a position in an HPPD protein, said position corresponding to position 392 of the amino acid sequence of SEQ ID No. 2;
m) Asp, Lys, or Asn at a position in an HPPD protein, said position corresponding to position 421 of the amino acid sequence of SEQ ID No. 2;
n) Ala or Gly at a position in an HPPD protein, said position corresponding to position 422 of the amino acid sequence of SEQ ID No. 2;
o) Ile, Arg or Ser at a position in an HPPD protein, said position corresponding to position 425 of the amino acid sequence of SEQ ID No. 2
p) Glu, Phe or Val at a position in an HPPD protein, said position corresponding to position 426 of the amino acid sequence of SEQ ID No. 2;
q) Ile, Met, Gln or Val at a position in an HPPD protein, said position corresponding to position 431 of the amino acid sequence of SEQ ID No. 2;
r) Ala, Cys, Thr, Val or Gly at a position in an HPPD protein, said position corresponding to position 228 of the amino acid sequence of SEQ ID No. 2;
s) Ala, Glu, His, Lys, Gln, Arg, Thr, Gly, Leu, Asn, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 248 of the amino acid sequence of SEQ ID No. 2;
t) Ala, Ile, Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 270 of the amino acid sequence of SEQ ID No. 2;
u) Ala, Glu, Lys, Arg, Ser, Thr, His, Ile, Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 271 of the amino acid sequence of SEQ ID No. 2;
v) His or Gln at a position in an HPPD protein, said position corresponding to position 379 of the amino acid sequence of SEQ ID No. 2; and
w) Leu or Arg at a position in an HPPD protein, said position corresponding to position 427 of the amino acid sequence of SEQ ID No. 2.

3. The nucleic acid of claim 1 or 2, wherein said at least one amino acid is selected from

a) Glu, Thr, Arg, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 2;
b) Ala or Val at a position in an HPPD protein, said position corresponding to position 269 of the amino acid sequence of SEQ ID No. 2;
c) Ala, Pro, Thr or Val at a position in an HPPD protein, said position corresponding to position 280 of the amino acid sequence of SEQ ID No. 2;
d) Ile or Met at a position in an HPPD protein, said position corresponding to position 335 of the amino acid sequence of SEQ ID No. 2;
e) Leu at a position in an HPPD protein, said position corresponding to position 368 of the amino acid sequence of SEQ ID No. 2;
f) Asp, Asn or Lys at a position in an HPPD protein, said position corresponding to position 421 of the amino acid sequence of SEQ ID No. 2;
g) Ala or Gly at a position in an HPPD protein, said position corresponding to position 422 of the amino acid sequence of SEQ ID No. 2;
h) Ala, Cys, Thr or Val at a position in an HPPD protein, said position corresponding to position 228 of the amino acid sequence of SEQ ID No. 2;
i) Ala, Glu, His, Lys, Gln, Arg, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 248 of the amino acid sequence of SEQ ID No. 2;
j) Ile, Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 270 of the amino acid sequence of SEQ ID No. 2;
k) Ala, Glu, Lys, Arg, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 271 of the amino acid sequence of SEQ ID No. 2;
l) His or Gln at a position in an HPPD protein, said position corresponding to position 379 of the amino acid

sequence of SEQ ID No. 2; and
m) Leu or Arg at a position in an HPPD protein, said position corresponding to position 427 of the amino acid sequence of SEQ ID No. 2.

4. The isolated nucleic acid of any one of claims 1 to 3, wherein said HPPD protein is derived from Streptomyces avermitilis
(Genebank SAV11864), Daucus carota (Genebank DCU 87257), Arabidopsis thaliana (Genebank AF047834), Mycosphaerella graminicola (Genebank AF038152), oryza sativa / rice [BAD26248], Zea mays / corn [ACN36372], avena sativa [ABZ23427], Pseudomonas fluorescens [ABF50055], Synechococcus sp. [YP_473959], Blepharisma japonicum [BAF91881], Rhodococcus RHA1 sp. ro0240 [YP_702005], Rhodococcus RHA1 sp. ro0341 [YP_703002], Picrophilus torridus [YP_024147], Kordia algicida [ZP_02161490], Sorghum bicolor [XP_002453359], Triticum aestivum / wheat [AAZ67144], or Hordeum vulgare / barley [O48604].

5. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 4 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr, at position 247 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 250 of SEQ ID No. 2);
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser, at position 248 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 251 of SEQ ID No. 2);
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at position 249 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 252 of SEQ ID No. 2) ;
d) Ala, His, Gln, Trp or Val,at position 250 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 253 of SEQ ID No. 2);
e) Val at position 262 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg or Tyr, at position 265 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 266 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 269 of SEQ ID No. 2);
h) Ala, Ile, Asn, Thr or Val at position 277 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val, at position 290 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 291 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 294 of SEQ ID No. 2);
k) Ile, Met or Asn at position 332 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 335 of SEQ ID No. 2);
l) Tyr at position 378 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 389 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 416 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 419 of SEQ ID No. 2);
o) Asp or Asn, at position 418 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 421 of SEQ ID No. 2);
p) Ala, Met, Pro or Thr at position 419 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 421 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro or Arg, at position 422 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 425 of SEQ ID No. 2);
s) Phe, Thr or Val, at position 423 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 426 of SEQ ID No. 2);
t) Met, Gln or Val at position 428 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at position 225 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 228 of SEQ ID No. 2);
v) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 245 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Met or Val at position 267 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 270 of SEQ ID No. 2);

x) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 268 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 271 of SEQ ID No. 2);
y) His at position 376 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at a position in an HPPD protein, said position corresponding to position 424 of the amino acid sequence of SEQ ID No. 4 (corresponding to position 427 of SEQ ID No. 2).

6. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 6 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 224 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 250 of SEQ ID No. 2);
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at position 225 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 251 of SEQ ID No. 2);
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at position 226 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 252 of SEQ ID No. 2);
d) Ala, His, Gln, Val or Trp at position 227 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 253 of SEQ ID No. 2);
e) Val at position 239 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val or Tyr at position 242 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 243 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 269 of SEQ ID No. 2);
h) Ala, Ile, Asn, Thr or Val at position 254 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val at position 267 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 268 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 294 of SEQ ID No. 2);
k) Ile or Asn at position 309 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 335 of SEQ ID No. 2);
l) Tyr at position 355 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 366 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 393 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 419 of SEQ ID No. 2);
o) Asp or Asn at position 395 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 421 of SEQ ID No. 2);
p) Ala, Met, Pro or Thr at position 396 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 398 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro or Arg at position 399 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 425 of SEQ ID No. 2);
s) Glu, Phe, Thr or Val at position 400 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 426 of SEQ ID No. 2);
t) Met, Gln or Val at position 405 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 202 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 228 of SEQ ID No. 2);
v) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 222 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Met or Val at position 244 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 270 of SEQ ID No. 2);
x) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 245 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 271 of SEQ ID No. 2);
y) Gln at position 353 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at position 401 of the amino acid sequence of SEQ ID No. 6 (corresponding to position 427 of SEQ ID No. 2).

7. The isolated nucleic acid of any one of claims 1 to 4, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 8 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 241 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 250 of SEQ ID No. 2), preferably Ala ;
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at position 242 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at position 243 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 252 of SEQ ID No. 2), preferably Tyr;
d) Ala, His, Gln, Val or Trp at position 244 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val at position 256 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg or Tyr at position 259 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 260 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 271 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val at position 284 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 285 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 294 of SEQ ID No. 2);
k) Ile at position 326 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 335 of SEQ ID No. 2);
1) Tyr at position 372 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 383 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 410 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 419 of SEQ ID No. 2);
o) Asp or Asn at position 412 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
p) Ala, Met, Pro or Thr at position 413 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 415 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro or Arg at position 416 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 425 of SEQ ID No. 2);
s) Phe, Thr or Val at position 417 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 426 of SEQ ID No. 2);
v) Met, Gln, or Val at position 422 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 431 of SEQ ID No. 2).
w) Ala, Cys, Gly or Thr at position 219 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 228 of SEQ ID No. 2);
x) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 239 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 248 of SEQ ID No. 2);
y) Ala, Ile, Met or Val at position 261 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 270 of SEQ ID No. 2);
z) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 262 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 271 of SEQ ID No. 2);
aa)His at position 370 of the amino acid sequence of SEQ ID No. 8 (corresponding to position 379 of SEQ ID No. 2); and
bb)Arg at position 418 of the amino acid sequence of SEQ ID No. 8
(corresponding to position 427 of SEQ ID No. 2).

8. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 10 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Phe, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 188 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 250 of SEQ ID No. 2);
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro or Ser at position 189 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 251 of SEQ ID No. 2), preferably Ala or Lys;

c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Glu at position 190 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 252 of SEQ ID No. 2), preferably Ser;
d) Ala, His, Gln, Val or Trp at position 191 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 253 of SEQ ID No. 2), preferably Phe or Val;
e) Val at position 200 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val or Tyr at position 203 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 268 of SEQ ID No. 2);
g) Thr or Val at position 204 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 269 of SEQ ID No. 2), preferably Val;
h) Ala, Ile, Asn, Thr or Val at position 215 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val at position 226 of the amino acid sequence of SEQ ID NO:SEQ ID No. 10 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 227 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 294 of SEQ ID No. 2);
k) Ile or Asn at position 264 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 335 of SEQ ID No. 2);
l) Tyr at position 312 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 321 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 333 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 419 of SEQ ID No. 2);
o) Asp, Lys or Asn at position 335 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
p) Ala, Met, Pro or Thr at position 336 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 338 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 424 of SEQ ID No. 2);
r) Ile or Pro at position 339 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 425 of SEQ ID No. 2);
s) Phe, Thr or Val at position 340 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 426 of SEQ ID No. 2);
t) Met, Gln or Val at position 345 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 431 of SEQ ID No. 2)
u) Ala, Cys, Gly or Val at position 164 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 228 of SEQ ID No. 2);
v) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Ser, Thr or Tyr at position 186 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Leu or Val at position 205 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 270 of SEQ ID No. 2);
x) Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Thr or Val at position 206 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 271 of SEQ ID No. 2);
y) His at position 310 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at position 341 of the amino acid sequence of SEQ ID No. 10 (corresponding to position 427 of SEQ ID No. 2).

9. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 14 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 169 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 250 of SEQ ID No. 2), preferably Ala or Phe;
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at position 170 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 251 of SEQ ID No. 2), preferably Ala, Arg or Lys;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Ser, Val or Tyr at position 171 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 252 of SEQ ID No. 2), preferably Glu, Ser or Tyr;
d) Ala, Phe, His, Gln or Val at position 172 of the amino acid sequence of SEQ ID No. 14 (corresponding to

position 253 of SEQ ID No. 2), preferably Phe or Val;
e) Val at position 181 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg or Tyr at position 184 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 185 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 269 of SEQ ID No. 2), preferably Ala ;
h) Ile, Asn, Pro, Thr or Val at position 196 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 280 of SEQ ID No. 2), preferably Pro;
i) Leu or Val at position 206 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 207 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 294 of SEQ ID No. 2);
k) Ile, Met or Asn at position 244 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
l) Phe or Tyr at position 301 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 312 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 325 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 419 of SEQ ID No. 2);
o) Asp, Lys or Asn at position 327 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
p) Gly, Met, Pro or Thr at position 328 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 330 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro, Arg or Ser at position 331 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 425 of SEQ ID No. 2);
s) Glu, Phe, Thr or Val at position 332 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
t) Ile, Met, Gln or Val at position 337 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at position 145 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 228 of SEQ ID No. 2);
v) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Ser, Thr or Tyr at position 167 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Leu or Met at position 186 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 270 of SEQ ID No. 2);
x) Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 187 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 271 of SEQ ID No. 2);
y) His at a position at position 299 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at a position at position 333 of the amino acid sequence of SEQ ID No. 14 (corresponding to position 427 of SEQ ID No. 2).

10. The isolated nucleic acid of claims 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 16 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr or Val at position 209 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 250 of SEQ ID No. 2), preferably Ala or Phe;
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at position 210 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 251 of SEQ ID No. 2), preferably Ala, Arg, Lys;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Val or Tyr at position 211 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 252 of SEQ ID No. 2), preferably Tyr;
d) Phe, His, Gln, Val or Trp at position 212 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 253 of SEQ ID No. 2), preferably Phe or Val;
e) Val at position 224 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 265 of SEQ ID

No. 2);
f) Leu, Gln, Arg or Tyr at position 227 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 228 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 239 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val at position 251 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 252 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 294 of SEQ ID No. 2);
k) Ile, Met or Asn at position 289 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
l) Tyr at position 336 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 347 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 359 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 419 of SEQ ID No. 2);
o) Asp, Lys or Asn at position 361 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
p) Ala, Met, Pro or Thr at position 362 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 364 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro, Arg or Ser at position 365 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 425 of SEQ ID No. 2);
s) Glu, Phe, Thr or Val at position 366 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
t) Ile, Met, Gln or Val at position 371 of the amino acid sequence of SEQ ID No. 16 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 185 of the amino acid sequence of SEQ ID No. 2 (corresponding to position 228 of SEQ ID No. 2);
v) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 207 of the amino acid sequence of SEQ ID No. 2 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Leu or Met at a position in an HPPD protein, said position corresponding to position 229 of the amino acid sequence of SEQ ID No. 2 (corresponding to position 270 of SEQ ID No. 2);
x) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 230 of the amino acid sequence of SEQ ID No. 2 (corresponding to position 271 of SEQ ID No. 2);
y) His at a position in an HPPD protein, said position corresponding to position 334 of the amino acid sequence of SEQ ID No. 2 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at a position in an HPPD protein, said position corresponding to position 367 of the amino acid sequence of SEQ ID No. 2 (corresponding to position 427 of SEQ ID No. 2).

11. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 18 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 231 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 250 of SEQ ID No. 2), preferably Phe or Ala;
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at position 232 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at position 233 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 252 of SEQ ID No. 2), preferably Ser or Tyr;
d) Ala, His, Gln, Val or Trp at position 234 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val at position 246 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val or Tyr at position 249 of the amino acid sequence of SEQ ID No. 18 (corresponding to

position 268 of SEQ ID No. 2);
g) Ala or Thr at position 250 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 261 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val at position 273 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 274 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 294 of SEQ ID No. 2);
k) Ile, Met or Asn at position 311 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
l) Tyr at position 356 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 367 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 379 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 419 of SEQ ID No. 2);
o) Asp, Lys or Asn at position 381 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
p) Ala, Met, Pro or Thr at position 382 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 384 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro, Arg or Ser at position 385 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 425 of SEQ ID No. 2);
s) Glu, Phe, Thr or Val at position 386 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
t) Met, Gln or Val at position 391 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 207 of the amino acid sequence of SEQ ID No. 1 (corresponding to position 228 of SEQ ID No. 2)8;
v) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 229 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Leu or Met at a position in an HPPD protein, said position corresponding to position 251 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 270 of SEQ ID No. 2);
x) Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Thr or Val at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 271 of SEQ ID No. 2);
y) His at a position in an HPPD protein, said position corresponding to position 354 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at a position in an HPPD protein, said position corresponding to position 387 of the amino acid sequence of SEQ ID No. 18 (corresponding to position 427 of SEQ ID No. 2).

12. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 30 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 232 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 250 of SEQ ID No. 2), preferably Phe or Ala;
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at position 233 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at position 234 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 252 of SEQ ID No. 2), preferably Ser or Tyr;
d) Ala, His, Gln, Val or Trp at position 235 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val at position 247 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val or Tyr at position 250 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 251 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 269 of

SEQ ID No. 2), preferably Ala;

h) Ala, Ile, Asn, Thr or Val at position 262 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 280 of SEQ ID No. 2);

i) Leu or Val at position 274 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 293 of SEQ ID No. 2);

j) Met at position 275 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 294 of SEQ ID No. 2);

k) Ile, Met or Asn at position 312 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 335 of SEQ ID No. 2), preferably Met;

l) Tyr at position 357 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 381 of SEQ ID No. 2);

m) Ser at position 368 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 392 of SEQ ID No. 2);

n) Tyr at position 380 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 419 of SEQ ID No. 2);

o) Asp, Lys or Asn at position 382 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;

p) Ala, Met, Pro or Thr at position 383 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 422 of SEQ ID No. 2);

q) Ala, Ile or Val at position 385 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 424 of SEQ ID No. 2);

r) Ile, Pro, Arg or Ser at position 386 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 425 of SEQ ID No. 2);

s) Glu, Phe, Thr or Val at position 387 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;

t) Met, Gln or Val at position 392 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 431 of SEQ ID No. 2);

u) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 208 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 228 of SEQ ID No. 2);

v) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser or Tyr at a position in an HPPD protein, said position corresponding to position 230 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 248 of SEQ ID No. 2);

w) Ala, Ile, Leu or Met at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 270 of SEQ ID No. 2);

x) Glu, His, Ile, Lys, Leu, Met, Arg, Thr or Val at a position in an HPPD protein, said position corresponding to position 253 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 271 of SEQ ID No. 2);

y) His at a position in an HPPD protein, said position corresponding to position 355 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 379 of SEQ ID No. 2); and

z) Arg at a position in an HPPD protein, said position corresponding to position 388 of the amino acid sequence of SEQ ID No. 30 (corresponding to position 427 of SEQ ID No. 2).

13. The isolated nucleic acid of claims 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 20 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 201 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 250 of SEQ ID No. 2), preferably Phe or Ala;

b) Ala, Asp, Glu, Lys, Leu, Asn, Pro, Arg or Ser at position 202 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 251 of SEQ ID No. 2), preferably Ala, Arg or Lys;

c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at position 203 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 252 of SEQ ID No. 2), preferably Glu, Ser or Tyr;

d) Ala, His, Gln, Val or Trp at position 204 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 253 of SEQ ID No. 2), preferably Val;

e) Val at position 216 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 265 of SEQ ID No. 2);

f) Leu, Gln, Arg, Val or Tyr at position 219 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 268 of SEQ ID No. 2);

g) Ala or Thr at position 220 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;

h) Ala, Ile, Asn, Thr or Val at position 230 of the amino acid sequence of SEQ ID No. 20 (corresponding to

position 280 of SEQ ID No. 2);
i) Leu or Val at position 242 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 243 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 294 of SEQ ID No. 2);
k) Ile, Met or Asn at position 280 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
l) Phe or Tyr at position 323 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 334 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 346 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 419 of SEQ ID No. 2);
o) Asp or Lys at position 348 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
p) Ala, Met, Pro or Thr at position 349 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 351 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro, Arg or Ser at position 352 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 425 of SEQ ID No. 2);
s) Glu, Phe, Thr or Val at position 353 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
t) Met, Gln, Phe or Val at position 358 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at position 177 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 228 of SEQ ID No. 2);
v) Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 199 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Leu or Met at a position at position 221 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 270 of SEQ ID No. 2);
x) Ala, Glu, His, Ile, Leu, Met, Arg, Ser, Thr or Val at position 222 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 271 of SEQ ID No. 2);
y) His at position 321 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at position 354 of the amino acid sequence of SEQ ID No. 20 (corresponding to position 427 of SEQ ID No. 2).

14. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 22 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Phe, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 219 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 250 of SEQ ID No. 2), preferably Phe or Ala;
b) Ala, Asp, Glu, Lys, Leu, Asn, Pro, Arg or Ser at position 220 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 251 of SEQ ID No. 2), preferably Ala, Arg or Lys;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Val or Tyr at position 221 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 252 of SEQ ID No. 2), preferably Glu or Tyr;
d) Ala, His, Gln, Val or Trp at position 222 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val at position 234 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val or Tyr at position 237 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 238 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 249 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val at position 261 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 293 of

SEQ ID No. 2);
j) Met at position 262 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 294 of SEQ ID No. 2);
k) Ile, Met or Asn at position 299 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
l) Tyr at position 342 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 353 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 365 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 419 of SEQ ID No. 2);
o) Asp, Lys or Asn at position 367 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 421 of SEQ ID No. 2), preferably Lys;
p) Ala, Met, Pro or Thr at position 368 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 370 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro, Arg or Ser at position 371 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 425 of SEQ ID No. 2);
s) Glu, Phe, Thr or Val at position 372 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 426 of SEQ ID No. 2), preferably Glu;
t) Met, Gln or Val at position 377 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at position 195 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 228 of SEQ ID No. 2);
v) Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 217 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Leu or Val at position 239 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 270 of SEQ ID No. 2);
x) Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Thr or Val at position 240 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 271 of SEQ ID No. 2);
y) His at a position at position 340 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at a position at position 373 of the amino acid sequence of SEQ ID No. 22 (corresponding to position 427 of SEQ ID No. 2).

15. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 24 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 241 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 250 of SEQ ID No. 2), preferably Ala;
b) Asp, Glu, Lys, Leu, Asn, Pro, Arg or Ser at position 242 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Val, or Tyr at position 243 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 252 of SEQ ID No. 2), preferably Tyr;
d) Ala, His, Gln, Val or Trp at position 244 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val at position 256 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val or Tyr at position 259 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 260 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 271 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val at position 284 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 285 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 294 of SEQ ID No. 2);

k) Ile or Asn at position 326 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 335 of SEQ ID No. 2);
l) Tyr at position 372 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 381 of SEQ ID No. 2);
m) Ser at position 383 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 410 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 419 of SEQ ID No. 2);
o) Asp or Asn at position 412 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 421 of SEQ ID No. 2);
p) Ala, Met, Pro or Thr at position 413 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 415 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro or Arg at position 416 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 425 of SEQ ID No. 2);
s) Phe, Thr or Val at position 417 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 426 of SEQ ID No. 2);
t) Met, Gln or Val at position 422 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at position 219 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 228 of SEQ ID No. 2);
v) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 239 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Met or Val at position 261 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 270 of SEQ ID No. 2);
x) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 262 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 271 of SEQ ID No. 2);
y) His at position 370 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at position 418 of the amino acid sequence of SEQ ID No. 24 (corresponding to position 427 of SEQ ID No. 2).

16. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 26 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 237 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 250 of SEQ ID No. 2), preferably Ala;
b) Asp, Glu, Lys, Leu, Asn, Pro, Arg or Ser at position 238 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 251 of SEQ ID No. 2), preferably Arg or Lys;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Val or Tyr at position 239 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 252 of SEQ ID No. 2), preferably Tyr;
d) Ala, His, Gln, Val or Trp at position 240 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 253 of SEQ ID No. 2), preferably Val;
e) Val at position 252 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 265 of SEQ ID No. 2);
f) Leu, Gln, Arg, Val or Tyr at position 255 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 268 of SEQ ID No. 2);
g) Ala or Thr at position 256 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 269 of SEQ ID No. 2), preferably Ala;
h) Ala, Ile, Asn, Thr or Val at position 267 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 280 of SEQ ID No. 2);
i) Leu or Val at position 280 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 293 of SEQ ID No. 2);
j) Met at position 281 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 294 of SEQ ID No. 2);
k) Ile, Met or Asn at position 322 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 335 of SEQ ID No. 2), preferably Met;
l) Tyr at position 368 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 381 of SEQ ID No. 2);

m) Ser at position 379 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 392 of SEQ ID No. 2);
n) Tyr at position 406 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 419 of SEQ ID No. 2);
o) Asp or Asn at position 408 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 421 of SEQ ID No. 2);
p) Ala, Met, Pro or Thr at position 409 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 422 of SEQ ID No. 2);
q) Ala, Ile or Val at position 411 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 424 of SEQ ID No. 2);
r) Ile, Pro, Arg at position 412 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 425 of SEQ ID No. 2);
s) Phe, Thr or Val at position 413 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 426 of SEQ ID No. 2);
t) Met or Gln or Val at position 418 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 431 of SEQ ID No. 2);
u) Ala, Cys, Gly or Thr at a position in an HPPD protein, said position corresponding to position 215 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 228 of SEQ ID No. 2);
v) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 235 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 248 of SEQ ID No. 2);
w) Ala, Ile, Met or Val at position 257 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 270 of SEQ ID No. 2);
x) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 258 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 271 of SEQ ID No. 2);
y) His at a position at position 366 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 379 of SEQ ID No. 2); and
z) Arg at position 414 of the amino acid sequence of SEQ ID No. 26 (corresponding to position 427 of SEQ ID No. 2).

17. The isolated nucleic acid of claim 1, wherein said HPPD protein comprises the amino acid sequence of SEQ ID No. 2 and wherein the resulting amino acid sequence comprises at least one amino acid selected from

a) Ala, Asp, Glu, Gly, Lys, Gln, Arg, Ser, Thr, Val or Tyr at position 250 of the amino acid sequence of SEQ ID No. 2;
b) Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at position 251 of the amino acid sequence of SEQ ID No. 2;
c) Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at position 252 of the amino acid sequence of SEQ ID No. 2;
d) Ala, His, Gln, Val or Trp at position 253 of the amino acid sequence of SEQ ID No. 2;
e) Val at a position at position 265 of the amino acid sequence of SEQ ID No. 2;
f) Leu, Gln, Arg, Val or Tyr at position 268 of the amino acid sequence of SEQ ID No. 2;
g) Ala or Thr at position 269 of the amino acid sequence of SEQ ID No. 2;
h) Ala, Ile, Asn, Thr or Val at position 280 of the amino acid sequence of SEQ ID No. 2;
i) Leu or Val at position 293 of the amino acid sequence of SEQ ID No. 2;
j) Met at position 294 of the amino acid sequence of SEQ ID No. 2;
k) Ile or Asn at position 335 of the amino acid sequence of SEQ ID No. 2;
l) Tyr at position 381 of the amino acid sequence of SEQ ID No. 2;
m) Ser at position 392 of the amino acid sequence of SEQ ID No. 2;
n) Tyr at position 419 of the amino acid sequence of SEQ ID No. 2;
o) Asp or Asn at position 421 of the amino acid sequence of SEQ ID No. 2;
p) Ala, Met, Pro or Thr at position 422 of the amino acid sequence of SEQ ID No. 2;
q) Ala, Ile or Val at position 424 of the amino acid sequence of SEQ ID No. 2;
r) Ile, Pro or Arg at position 425 of the amino acid sequence of SEQ ID No. 2;
s) Phe, Thr or Val at position 426 of the amino acid sequence of SEQ ID No. 2;
t) Met, Gln or Val position 431 of the amino acid sequence of SEQ ID No. 2;
u) Ala, Cys, Gly or Thr at position 228 of the amino acid sequence of SEQ ID No. 2;
v) Ala, Glu, Gly, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at position 248 of the amino acid sequence of SEQ ID No. 2;
w) Ala, Ile, Met or Val at position 270 of the amino acid sequence of SEQ ID No. 2;
x) Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at position 271 of the amino acid sequence of SEQ ID No. 2;
y) His at position 379 of the amino acid sequence of SEQ ID No. 2; and

z) Arg at position 427 of the amino acid sequence of SEQ ID No. 2.

18. The nucleic acid of any one of claims 1 to 17, wherein in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises (positions corresponding to SEQ ID No. 2) (a) Glu, Ser or Tyr at position 252; (b) Val or Ala at position 269; (c) Pro, Val or Ala at position 280; (d) Asp, Lys or Asn at position 421; and (e) Gly or Ala at postion 422.

19. The nucleic acid of any one of claims 1 to 18, wherein in said mutated HPPD protein at least two amino acids have been replaced so that the resulting amino acid sequence comprises at least two amino acids selected from the amino acids at the positions listed in any one of claims 1 to 18.

20. An isolated nucleic acid comprising a nucleotide sequence encoding a mutated HPPD protein, wherein said mutated HPPD protein has HPPD activity, and wherein in said mutated HPPD protein at least one amino acid at position 228, 248, 270, 271, 379 and/or 427 (according to the numbering of SEQ ID No. 2) has been replaced by another amino acid.

21. The isolated nucleic acid of claim 20, wherein in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises at least one amino acid selected from

a. Ala, Cys, Gly, Thr or Val at a position in an HPPD protein, said position corresponding to position 228 of the amino acid sequence of SEQ ID No. 2;
b. Ala, Glu, Gly, His, Lys, Leu, Asn, Gln, Arg, Ser, Thr or Tyr at a position in an HPPD protein, said position corresponding to position 248 of the amino acid sequence of SEQ ID No. 2;
c. Ala, Ile, Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 270 of the amino acid sequence of SEQ ID No. 2;
d. Ala, Glu, His, Ile, Lys, Leu, Met, Arg, Ser, Thr or Val at a position in an HPPD protein, said position corresponding to position 271 of the amino acid sequence of SEQ ID No. 2;
e. His or Gln at a position in an HPPD protein, said position corresponding to position 379 of the amino acid sequence of SEQ ID No. 2; and
f. Leu or Arg at a position in an HPPD protein, said position corresponding to position 427 of the amino acid sequence of SEQ ID No. 2.

22. The isolated nucleic acid of claim 21 or 22, wherein in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises at least one amino acid selected from

a) Val or Thr at a position in an HPPD protein, said position corresponding to position 228 of the amino acid sequence of SEQ ID No. 2;
b) Leu, Met or Val at a position in an HPPD protein, said position corresponding to position 270 of the amino acid sequence of SEQ ID No. 2;
c) Ala or Ser at a position in an HPPD protein, said position corresponding to position 271 of the amino acid sequence of SEQ ID No. 2,
d) Gln at a position in an HPPD protein, said position corresponding to position 379 of the amino acid sequence of SEQ ID No. 2; and
e) Leu at a position in an HPPD protein, said position corresponding to position 427 of the amino acid sequence of SEQ ID No. 2.

23. The nucleic acid of any one of claims 1 to 22, wherein said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one herbicide acting on HPPD.

24. A protein encoded by the isolated nucleic acid of any one of claims 1 to 23.

25. A chimeric gene comprising a coding sequence comprising the nucleic acid of any one of claims 1 to 23 operably linked to a plant-expressible promoter and optionally a transcription termination and polyadenylation region.

26. A method of obtaining a mutated HPPD protein capable of modulating the tolerance of a plant to at least one herbicide acting on HPPD, wherein said mutated HPPD protein has HPPD activity, the method comprising

i) providing an HPPD protein;

ii) replacing at least one amino acid in said HPPD protein so that the resulting amino acid sequence comprises at least one selected from

a) Ala, Asp, Glu, Phe, Gly, Lys,Gln, Arg, Ser, Thr, Val or Tyr at a position in an HPPD protein, said position corresponding to position 250 of the amino acid sequence of SEQ ID No. 2;
b) Ala, Asp, Glu, Ile, Lys, Leu, Asn, Pro, Arg or Ser at a position in an HPPD protein, said position corresponding to position 251 of the amino acid sequence of SEQ ID No. 2;
c) Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Gln, Arg, Ser, Val or Tyr at a position in an HPPD protein, said position corresponding to position 252 of the amino acid sequence of SEQ ID No. 2;
d) Ala, Phe, His, Gln, Val or Trp at a position in an HPPD protein, said position corresponding to position 253 of the amino acid sequence of SEQ ID No. 2;
e) Leu or Val at a position in an HPPD protein, said position corresponding to position 265 of the amino acid sequence of SEQ ID No. 2;
f) Leu, Gln, Arg, Val or Tyr at a position in an HPPD protein, said position corresponding to position 268 of the amino acid sequence of SEQ ID No. 2;
g) Ala, Thr or Val at a position in an HPPD protein, said position corresponding to position 269 of the amino acid sequence of SEQ ID No. 2;
h) Ala, Ile, Asn, Pro, Thr or Val at a position in an HPPD protein, said position corresponding to position 280 of the amino acid sequence of SEQ ID No. 2;
i) Leu, Gln or Val at a position in an HPPD protein, said position corresponding to position 293 of the amino acid sequence of SEQ ID No. 2;
j) Ile or Met at a position in an HPPD protein, said position corresponding to position 294 of the amino acid sequence of SEQ ID No. 2;
k) Gln at a position in an HPPD protein, said position corresponding to position 307 of the amino acid sequence of SEQ ID No. 2;
l) Ile, Met or Asn at a position in an HPPD protein, said position corresponding to position 335 of the amino acid sequence of SEQ ID No. 2;
m) Leu at a position in an HPPD protein, said position corresponding to position 368 of the amino acid sequence of SEQ ID No. 2;
n) Phe or Tyr at a position in an HPPD protein, said position corresponding to position 381 of the amino acid sequence of SEQ ID No. 2;
o) Phe or Ser at a position in an HPPD protein, said position corresponding to position 392 of the amino acid sequence of SEQ ID No. 2;
p) Phe or Tyr at a position in an HPPD protein, said position corresponding to position 419 of the amino acid sequence of SEQ ID No. 2;
q) Asp, Phe, Lys, Asn at a position in an HPPD protein, said position corresponding to position 421 of the amino acid sequence of SEQ ID No. 2;
r) Ala, Gly, Met, Pro or Thr at a position in an HPPD protein, said position corresponding to position 422 of the amino acid sequence of SEQ ID No. 2;
s) Ala, Phe, Ile or Val at a position in an HPPD protein, said position corresponding to position 424 of the amino acid sequence of SEQ ID No. 2;
t) Ile, Pro, Arg or Ser at a position in an HPPD protein, said position corresponding to position 425 of the amino acid sequence of SEQ ID No. 2;
u) Glu, Phe, Thr or Val at a position in an HPPD protein, said position corresponding to position 426 of the amino acid sequence of SEQ ID No. 2;
v) Ile, Met, Gln or Val at a position in an HPPD protein, said position corresponding to position 431 of the amino acid sequence of SEQ ID No. 2; and
w) an amino acid deletion or replacement at at least one position in an HPPD protein, said position corresponding to at least one of positions 228, 248, 270, 271, 379 and 427 of the amino acid sequence of SEQ ID No. 2;

iii) determining the inhibition of the resulting HPPD protein by at least one herbicide acting on HPPD,
wherein an inhibition of the resulting protein of less or more than that observed with a reference HPPD protein is indicative that the resulting protein is capable of modulating the tolerance of a plant to said herbicide.

27. The method of claim 26, wherein said mutated HPPD protein is capable of increasing the tolerance of a plant to at least one HPPD inhibitor herbicide.

28. The nucleic acid of claim 23 or the method of claim 27, wherein the herbicide acting on HPPD is tembotrione.

29. A method of producing a transgenic plant comprising introducing into a said plant the nucleic acid of any one of claims 1 to 23 or a nucleic acid encoding the HPPD enzyme identified by the method of any one of claims 26 to 28, both operably linked to a plant expressible promoter or the chimeric gene of claim 25, and obtaining progeny thereof comprising said operably linked nucleic acid or said chimeric gene.

30. The method of claim 29, wherein the nucleic acid of claim 23 or a nucleic acid identified by the method of claim 27 or 28, both operably linked to a plant expressible promoter, or the chimeric gene of claim 25 comprising the nucleic acid of claim 23 is introduced into said plant.

31. The nucleic acid of any one of claims 1 to 23 or the method of any one of claims 26 to 30, wherein said HPPD protein comprises

a) a His at a position in an HPPD protein, said position corresponding to position 226 of the amino acid sequence of SEQ ID No. 2;
b) a Ser at a position in an HPPD protein, said position corresponding to position 267 of the amino acid sequence of SEQ ID No. 2;
c) an Asn at a position in an HPPD protein, said position corresponding to position 282 of the amino acid sequence of SEQ ID No. 2;
d) a His at a position in an HPPD protein, said position corresponding to position 308 of the amino acid sequence of SEQ ID No. 2;
e) a Tyr at a position in an HPPD protein, said position corresponding to position 342 of the amino acid sequence of SEQ ID No. 2;
f) a Glu at a position in an HPPD protein, said position corresponding to position 394 of the amino acid sequence of SEQ ID No. 2;
g) a Gly at a position in an HPPD protein, said position corresponding to position 420 of the amino acid sequence of SEQ ID No. 2; and
h) an Asn at a position in an HPPD protein, said position corresponding to position 423 of the amino acid sequence of SEQ ID No. 2

32. A plant cell comprising the isolated nucleic acid of any one of claims 1 to 23 or the chimeric gene of claim 25 in its genetic information.

33. A plant, part thereof or plant tissue consisting essentially of the plant cells of claim 32.

34. A plant obtainable from the method of any one of claims 29 or 30.

35. The plant of claim 33 or 34 which is selected from wheat, cotton, canola, rice, corn, soy bean, sorghum

36. A seed of the plant of any one of claims 33 to 35.

37. Progeny of the plant of any one of claims 33 to 35 or the seed of claim 36.

38. A method of modulating a plant's tolerance to at least one herbicide acting on HPPD or of obtaining a plant tolerant to an HPPD inhibitor herbicide comprising introducing the isolated nucleic acid of any one of claims 1 to 23 operably linked to a plant expressible promoter or the chimeric gene of claim 25 into a plant's genome.

39. A method for controlling weeds comprising spraying at least one HPPD inhibitor herbicide on or around a crop plant, wherein said crop plant contains the nucleic acid according to claim 23 operably linked to a plant expressible promoter or the chimeric gene of claim 25 comprising the nucleic acid of claim 23.

40. Use of a chimeric gene of claim 25 or the nucleic acid of any one of claims 1 to 23 operably linked to a plant expressible promoter for modulating the tolerance of a plant to at least one HPPD inhibitor herbicide applied for controlling weeds.

41. The method of claim 30, 38 or 39 or the use of claim 40, wherein the tolerance of a plant to at least one HPPD inhibitor herbicide is increased.

Figure 1a: Superpositon of the x-ray structure of HPPD from Arabidopsis thaliana (dark grey) and Pseudomonas fluorescens (light grey). The structure is shown as ribbon plot.

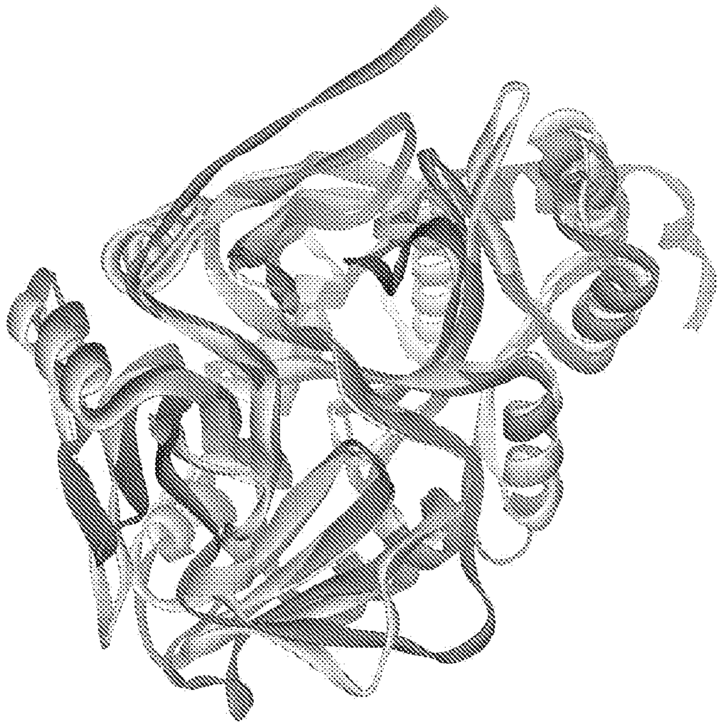


Figure 1b: Superpositon of the x-ray structure of HPPD from Arabidopsis thaliana (dark grey) and *Streptomyces avermitilis* (light grey). The structure is shown as ribbon plot.

Figure 1c: Superpositon of the x-ray structure of HPPD from Arabidopsis thaliana (dark grey) and *Homo sapiens* (light grey). The structure is shown as ribbon plot.

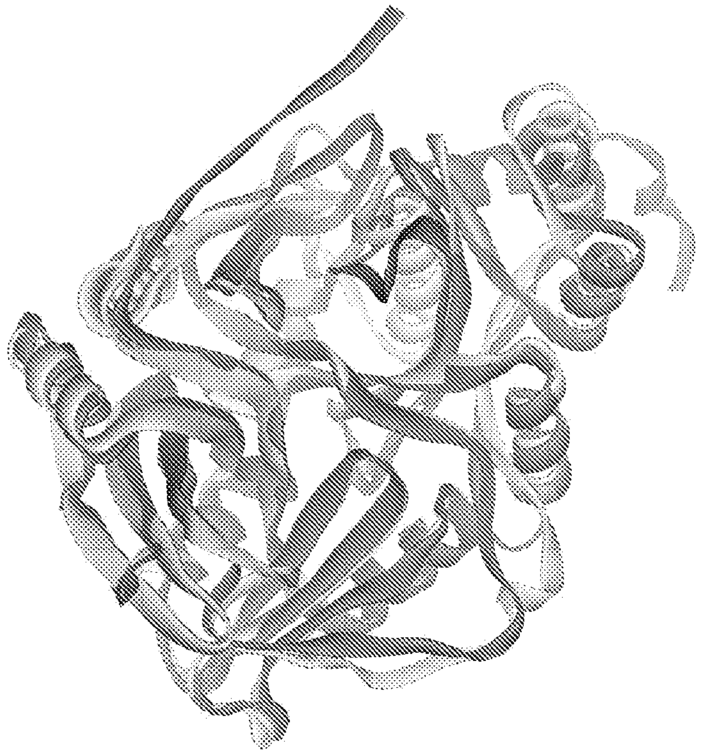


Figure 1d: Superpositon of the x-ray structure of HPPD from Arabidopsis thaliana (dark grey) and *Rattus norvegicus* (light grey). The structure is shown as ribbon plot.

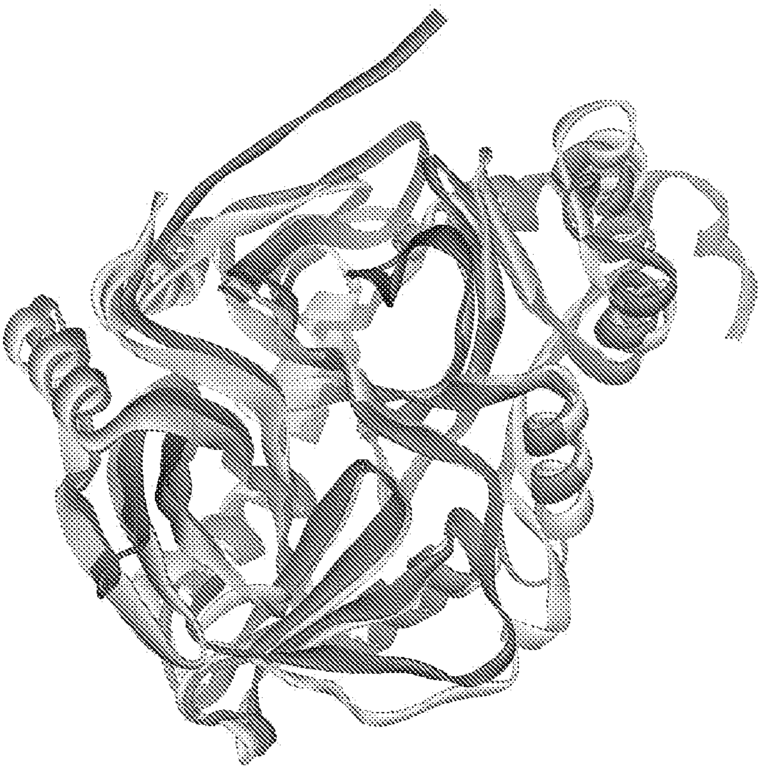


Figure 2a: Amino acids forming the binding site of *Arabidopsis thaliana* (represented by bold lines). The core of the HPPD protein from *Arabidopsis thaliana* is shown as C_{alpha} trace and the iron is marked.

Figure 2b: Amino acids forming the binding site of *Pseudomonas fluorescens* (represented by bold lines). The core of the HPPD protein from *Pseudomonas fluorescens* is shown as C_{alpha} trace and the iron is marked.

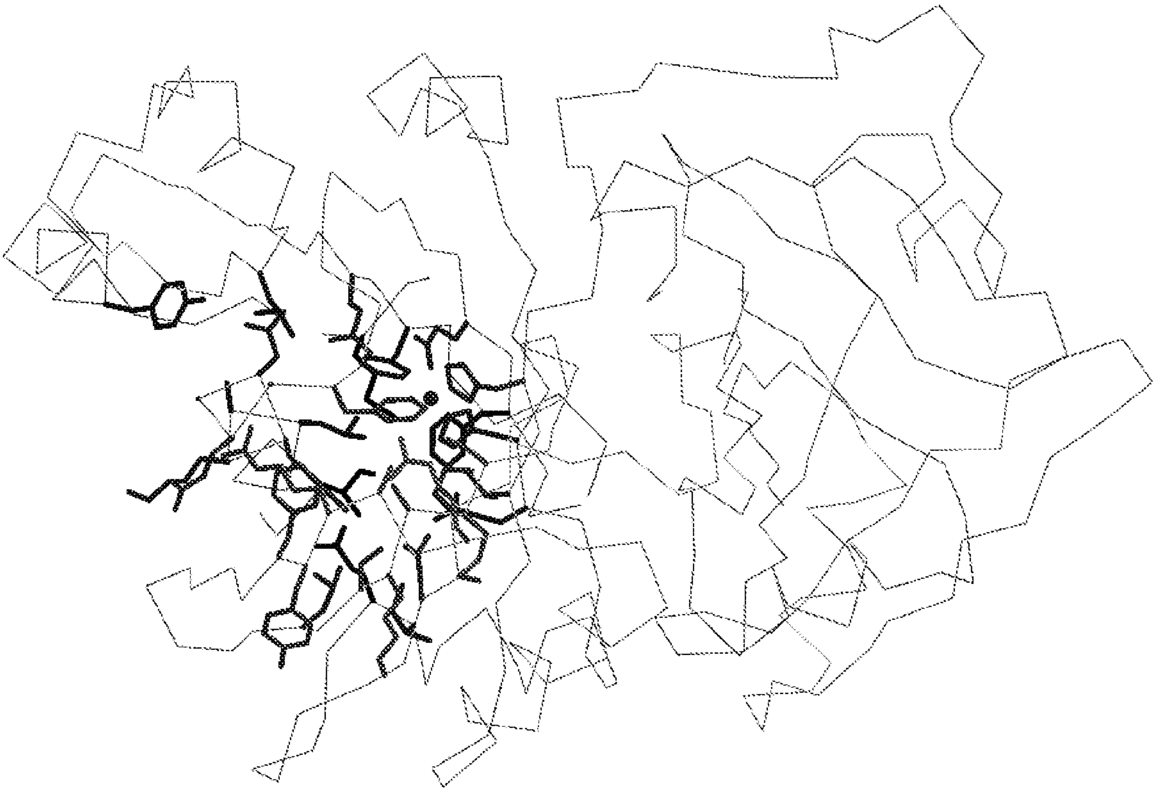


Figure 2c: Amino acids forming the binding site of *Streptomyces avermitilis* (represented by bold lines). The core of the HPPD protein from *Streptomyces avermitilis* is shown as C_{alpha} trace and the iron is marked.

Figure 2d: Amino acids forming the binding site of *Homo sapiens* (represented by bold lines). The core of the HPPD protein from *Homo sapiens* is shown as C_{alpha} trace and the iron is marked.

Figure 2e: Amino acids forming the binding site of *Rattus norvegicus* (represented by bold lines). The core of the HPPD protein from *Rattus norvegicus* is shown as C_{alpha} trace and the iron is marked.

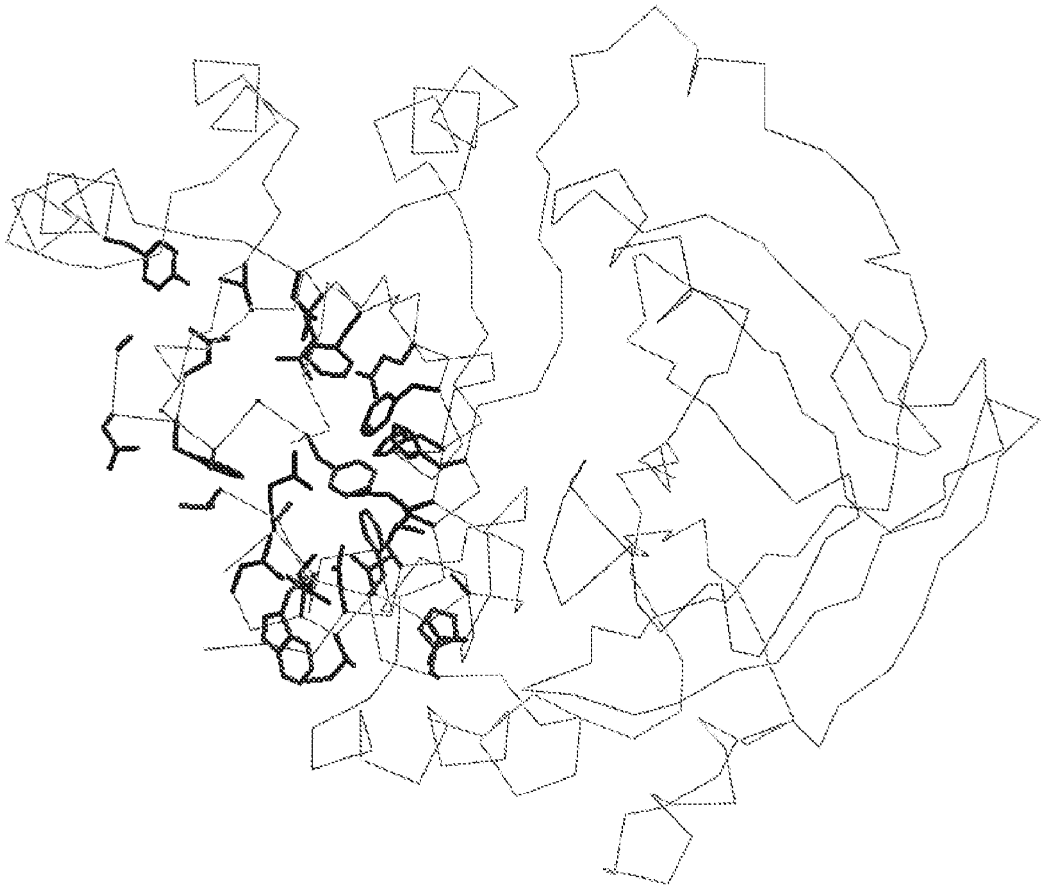
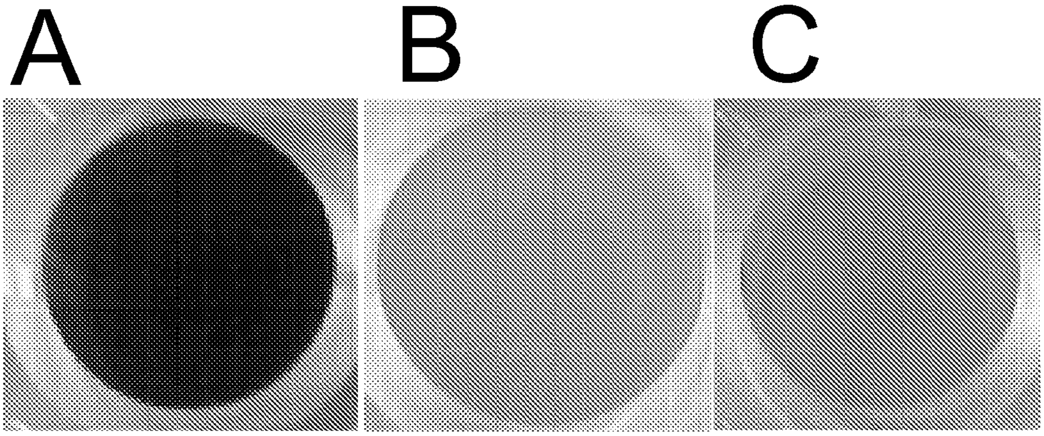


FIGURE 3: Brown test color.



A: WT, B:N282A, C: S267A

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EUROPEAN SEARCH REPORT

Application Number
EP 10 19 0629

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	WO 2009/144079 A1 (BAYER BIOSCIENCE NV [BE]; BAYER CROPSCIENCE AG [DE]; BUSCH MARCO [DE];) 3 December 2009 (2009-12-03) * page 5, paragraph 2 - page 6, paragraph 1; example 3 * -----	1,2, 4-17,19, 23-41	INV. C12N9/02 C12N15/82
A	WO 2010/085705 A2 (SYNGENTA PARTICIPATIONS AG [CH]; HAWKES TIMOTHY ROBERT [GB]; LANGFORD) 29 July 2010 (2010-07-29) -----	1,2, 4-17,19, 23-41	
A	WO 99/24585 A1 (RHONE POULENC AGROCHIMIE [FR]) 20 May 1999 (1999-05-20) * examples 3-8 * -----	1,2, 4-17,19, 23-41	
A	WO 02/46387 A2 (SYNGENTA LTD [GB]; WARNER SIMON ANTHONY JAMES [GB]; HAWKES TIMOTHY ROB) 13 June 2002 (2002-06-13) -----	1,2, 4-17,19, 23-41	
A	KAKIDANI HITOSHI ET AL: "Three-dimensional modeling of plant 4-hydroxyphenylpyruvate dioxygenase, a molecular target of triketone-type herbicides", JOURNAL OF PESTICIDE SCIENCE - NIPPON NOYAKU GAKKAISHI, NIPPON NOYAKU GAKKAI, TOKYO, JP, vol. 28, no. 4, 1 January 2003 (2003-01-01), pages 409-415, XP008100740, ISSN: 0385-1559 ----- -/--	1,2, 4-17,19, 23-41	TECHNICAL FIELDS SEARCHED (IPC) C12N

~~The present search report has been drawn up for all claims~~

Place of search	Date of completion of the search	Examiner
Munich	19 April 2011	Kania, Thomas

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons
....
& : member of the same patent family, corresponding document

2

EPO FORM 1503 03.82 (P04C01)

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EUROPEAN SEARCH REPORT

Application Number
EP 10 19 0629

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	FRITZE IRIS M ET AL: "The crystal structures of Zea mays and Arabidopsis 4-hydroxyphenylpyruvate dioxygenase", PLANT PHYSIOLOGY (ROCKVILLE), vol. 134, no. 4, April 2004 (2004-04), pages 1388-1400, XP002631689, ISSN: 0032-0889 -----	2,4-17, 19,23-41	
A	YANG CHENG ET AL: "Structural basis for herbicidal inhibitor selectivity revealed by comparison of crystal structures of plant and mammalian 4-hydroxyphenylpyruvate dioxygenases", BIOCHEMISTRY, vol. 43, no. 32, 17 August 2004 (2004-08-17), pages 10414-10423, XP002631690, ISSN: 0006-2960 -----	1,2, 4-17,19, 23-41	
			TECHNICAL FIELDS SEARCHED (IPC)

~~The present search report has been drawn up for all claims~~

2

Place of search	Date of completion of the search	Examiner
Munich	19 April 2011	Kania, Thomas

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons
&: member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

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Application Number

EP 10 19 0629

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

see additional sheet(s)

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

LACK OF UNITY OF INVENTION SHEET B

Application Number
EP 10 19 0629

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1, 2, 4-17, 19, 23-41(all partially)

An isolated nucleic acid comprising a nucleotide sequence encoding a mutated HPPD protein, wherein said mutated HPPD protein has HPPD activity , and wherein in said mutated HPPD protein at least one amino acid has been replaced so that the resulting amino acid sequence comprises at least one amino acid selected from Ala, Glu, Phe, Gly, Lys, Gln, Ard, Ser, Thr, Val or Tyr at a position in an HPPD protein, said position corresponding to position 250 of the amino acid sequence of SEQ ID NO:2, as well as related subject-matter as claimed.

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2. claims: 1, 2, 4-17, 19, 23-41(all partially)

idem for position 251

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3. claims: 1-19, 23-41(all partially)

idem for position 252

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4. claims: 1, 2, 4-17, 19, 23-41(all partially)

idem for position 253

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5. claims: 1, 2, 4-17, 19, 23-41(all partially)

idem for position 265

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6. claims: 1, 2, 4-17, 19, 23-41(all partially)

idem for position 268

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7. claims: 1-19, 23-41(all partially)

idem for position 269

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8. claims: 1-19, 23-41(all partially)

idem for position 280

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9. claims: 1, 4-17, 19, 23-41(all partially)

LACK OF UNITY OF INVENTION SHEET B

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

idem for position 293

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10. claims: 1, 4-17, 19, 23-41(all partially)

idem for position 294

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11. claims: 1, 2, 4, 19, 23-41(all partially)

idem for position 307

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12. claims: 1-19, 23-41(all partially)

idem for position 335

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13. claims: 1-4, 19, 23-41(all partially)

idem for position 368

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14. claims: 1, 4-19, 23-41(all partially)

idem for position 381

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15. claims: 1, 2, 4-17, 19, 23-41(all partially)

idem for position 392

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16. claims: 1, 4-17, 19, 23-41(all partially)

idem for position 419

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17. claims: 1-19, 23-41(all partially)

idem for position 421

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18. claims: 1-19, 23-41(all partially)

idem for position 422

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19. claims: 1, 4-17, 19, 23-41(all partially)

idem for position 424

LACK OF UNITY OF INVENTION SHEET B

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

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20. claims: 1, 2, 4-17, 19, 23-41(all partially)

    idem for position 425

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21. claims: 1, 2, 4-17, 19, 23-41(all partially)

    idem for position 426

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22. claims: 1, 2, 4-17, 19, 23-41(all partially)

    idem for position 431

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23. claims: 1, 2, 4-17, 19-41(all partially)

    idem for position 228

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24. claims: 1, 2, 4-17, 19-21, 23-41(all partially)

    idem for position 248

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25. claims: 1, 2, 4-17, 19-41(all partially)

    idem for position 270

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26. claims: 1, 2, 4-17, 19-41(all partially)

    idem for position 271

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27. claims: 1, 2, 4-17, 19-41(all partially)

    idem for position 379

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28. claims: 1, 2, 4-17, 19-41(all partially)

    idem for position 427

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 10 19 0629

19-04-2011

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